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THE PATHOGENESIS AND MANAGEMENT OF SPINAL MYELOMENINGOCELE.[1]

By E. DURHAM SMITH, F.R.A.C.S.,
Melbourne.

THIS paper presents the results of an investigation into the natural history, pathology and treatment of children suffering from spina bifida cystica. The study involved the follow-up investigation of 214 children who presented themselves at the Royal Children's Hospital, Melbourne, over a fifteen-year period ending in June, 1958. Only that type of spina bifida associated with a visible cystic or solid mass on the back is discussed, and no mention is made of spina bifida occulta. In this series of 214 patients, the common lesion was unfortunately the one with neurological disability, 183 of the patients having myelomeningoceles and the remainder having simple meningoceles. The over-all fate of 183 myelomeningocele patients is that 119 (68%) are now dead and 56 (32%) alive.

In this study, all the living children had been personally examined, and with patients who had presented since June, 1958, about 80 living children were currently being treated for this condition. In addition, many of the children who had recently died had been personally examined.

About 80 infants with a myelomeningocele were born in Victoria in each year. However, the problem was not only one of considerable frequency, but in addition, in those who survived, the disabilities were very severe. In the first 56 surviving children, only one child has normal urinary control and only nine children have a normal locomotor state. There was major orthopædic disability in 29 and minor disability in 18. The bowel was incontinent in all except four patients, and hydrocephalus had been present in 25. These figures indicated that the decisions about management involved serious problems of several systems—namely, the urinary tract, the bowel, paralysed limbs, hydrocephalus—as well as problems associated with sensory loss such as pressure sores and vasomotor phenomena. In addition, there were long-term problems of education and total rehabilitation to useful open employment.

In this immense field, only one aspect of management of immediate interest to the pædiatrician has been selected for discussion—namely, the management of the new-born child with a cystic mass on the back. Should the pædiatrician refer the baby to the surgeon for operation? If so, when should he be operated upon? What are the factors which influence the pædiatrician's decision about management in the first few weeks?

[1] Read at a meeting of the Australian Pædiatric Association, Canberra, April 22 to 25, 1960.

To answer these questions, several features of the pathology of the disease as they appeared from dissections and observations during operation are described.

About 50% of all infants with myelomeningocele died in the first six weeks after birth and most of the remainder within the first year. The deaths in this period were due almost exclusively to progressive hydrocephalus with or without meningitis. After the first year, death was usually due to problems associated with the neurogenic bladder. In the first few weeks, therefore, the emphasis in management must be on the management of hydrocephalus and meningitis.

The Pathology of the Spinal Cord and Spinal Roots.

The primary lesion in a myelomeningocele was found to be dysplasia of the spinal cord. Apart from the other pathological features, such as the presence of skin ulceration, the involvement of spinal roots in the meningeal sac, etc., it was in the cord itself that the pathogenesis of the clinical signs could be found.

Four basic types of dysplasia were found to exist. First, the cord may be split—that is, it remains in the early embryonic stage of an open neural plate. The usual word for this anomaly is rachischisis, although a better name would be myeloschisis. Many of these infants were stillborn, and the condition is sometimes associated with anencephalus. Secondly, the cord may be solid, but degenerate and necrotic. A typical dissection showed a solid necrotic cord, and it was noted that the peripheral spinal roots were macroscopically normal even where they emerged from the area of dysplasia. Thirdly, the cord may be cystic and cavitated. Such cystic areas may concern only a dilatation of the central canal of the spinal cord—a condition known as hydromyelia. At other times there may be multiple cystic cavities in the dysplasic cord—a condition well described as myelocystocele. The latter condition is probably derived from an extension of a hydromyelic cavity. It was noted again that the peripheral roots were macroscopically normal even from these areas of dysplasic cord. Fourthly, the cord may be proliferated and, occasionally, quite enormous proliferation of neural tissue can be seen. All surgeons have experienced the difficulty that is sometimes encountered in trying to replace this type of neural tissue in the spinal canal, and even laminectomy has sometimes not given sufficient space to accommodate all the neural tissue.

From a study of these pathological features three conclusions could be drawn.

1. Any theory of pathogenesis must explain these four varieties of cord abnormality, not including even the simple meningocele when the cord is normal. Thus, any theory of pathogenesis has to explain a split unfused neural plate, a solid fused neural tube, a hydromyelic or cystic cord and a proliferated cord. It is apparent, therefore, that no simple theory of pathogenesis is adequate. In another paper (Durham Smith, 1959) I have reviewed the evidence for each of the several hypotheses of pathogenesis, and they are not discussed in the present paper.

2. The normality of the peripheral spinal roots, and especially the constant presence of sensory nerve roots even from areas of dysplasic cord, suggest that the embryological site of the lesion is in the neural plate and not in the neural crest tissue.

3. As the basic lesion is dysplasia of the central nervous system, which is an irreversible state, operation on the myelomeningocele mass can be looked upon as of cosmetic value only.

The Meninges and Meningitis.

When some of the huge ulcerated masses seen in myelomeningoceles are observed, it must often be wondered why the patients do not all develop meningitis, especially so when dissections have shown that in the ulcerated lesions the dura terminates at the skin edge and only the arachnoid membrane covers the neural elements. However, dissections have shown that although some patients have a sac filled with cerebro-spinal fluid in continuity with the subarachnoid space of the spinal canal, often there is close adherence of the cord with the meninges at the neck of the sac, actually sealing off the subarachnoid space. This process of sealing-off may be almost complete in cases in which proliferated, bulky, spinal cord masses practically fill the sac. It is this fact of adherence of nerve elements to arachnoid membrane which may account for the lower incidence of meningitis in association with ulcerated meningoceles than one would have expected from the infected nature of the surface.

The incidence of meningitis in this series showed that the over-all risk of meningitis in ulcerated myelomeningoceles was about one case in three, or 35%. This may be compared with McNab's figure of 18% in 150 cases of ulcerated myelomeningocele (1958). It was also shown that antibiotics given parenterally were of very little prophylactic use in the prevention of meningitis, although the figures were probably too small for any certain conclusion to be drawn. Although some patients were prevented from developing meningitis by the anatomical sealing-off of the subarachnoid space, a 35% risk was, however, a considerable one. The real dangers of meningitis, apart from actually killing the child, have been as follows: (i) worsening of the neurological state by reason of ascending myelitis and thrombophlebitis; (ii) the development of adhesions, which may contribute to further blockage of the subarachnoid space, and thus further complicate or aggravate the hydrocephalus.

Whereas experience has shown that antibiotics given parenterally are of doubtful prophylactic value in protecting the patient with an ulcerated myelomeningocele against meningitis, there is considerable evidence that operation on the myelomeningocele mass shortly after birth was of definite prophylactic value. Of 33 patients operated upon in the first month, all of them having myelomeningoceles with an incomplete skin cover, only three developed meningitis. Therefore, this would seem to be an important consideration in the early management of these patients.

Hydrocephalus.

There was much evidence to suggest that probably all patients with a myelomeningocele have or have had some degree of hydrocephalus. Some may have compensated in utero or in early post-natal life, and the condition may not be apparent. In this series, 77% of the patients had clinical, ventriculographic or autopsy evidence of hydrocephalus.

The natural history of the hydrocephalic patients showed that there was an extremely bad prognosis when hydrocephalus was left to its spontaneous course. Two facts have emerged from a study of the natural history of hydrocephalus associated with myelomeningocele.

1. Untreated, of all those patients who developed hydrocephalus only one in five survived. This was a basic fact to be considered in the early decisions about management, and would suggest that there is a place for more energetic operative attack on the hydrocephalus if survival figures are to improve.

2. Conversely, some patients have spontaneously compensated and survived. This fact must therefore modify any view which advocates the insertion of a ventriculo-atrial valve shunt in every hydrocephalic who presents.

Finally, of relevance to the timing of any operative procedure, it is important to know when the risk of hydrocephalus declaring itself is virtually finalized. It has been demonstrated that in the majority of hydrocephalics, hydrocephalus is present at birth, and that over 90% of all hydrocephalics reveal themselves by the fifth or sixth week after birth. Thus, if hydrocephalus is not present by the end of the second month, with only rare exceptions does it show itself at a later period.

Ætiology.

Inquiries were made from 179 families, and no evidence of any abnormal exogenous influence in pregnancy, such as infections, drugs, X rays, diet, etc., could be elicited This

is not surprising, when it is realized that the neural tube has closed over already by the fourth week, and any exogenous influence would have to be introduced within this time and be remembered by the mother very early in pregnancy. In fact, the disease had commenced before the mother realized she was pregnant. The one positive aetiological feature was the family history. It was shown that the incidence of myelomeningocele in a second sibling within the same family was 7·8%. When, to this, was added the incidence of other congenital anomalies in siblings (a further 2·4%), the risk taken by such a family in having a further child is seen to be considerable.

Management.

In the light of these observations, some conclusions about the place and timing of any operation on the myelomeningocele mass itself can be made. There are two fairly extreme views as to the timing of operation. The first, held by many surgeons, particularly neurosurgeons, is that operation should be delayed for as long as possible, at least for some months. On the other hand, there is a strong conviction in many centres of the world that the elective time for operation is immediately after birth.

There are difficulties about both these positions, and my proposal is to make the decision about operation at about the fifth or sixth week after birth. Several factors may still prevent operation at this time, but it has been the aim to do so if at all possible. The reason for choosing this particular time for a definitive assessment and decision is discussed by an analysis of the other two positions.

Delayed Operation.

It is true that some myelomeningoceles do not require operation at all—for example, a small mass soundly covered by skin with minimal neurological disability, or even a large ulcerated mass, provided it is flat and showing good evidence of epithelial ingrowth. In the latter case the mass will eventually be covered by skin, and the only advantage of operation would be a better cosmetic result. However, the main basis of the preference for delayed operation is that the process of natural selection should be allowed to run its course, so that surgery is offered only to those who have proved that survival is possible—in other words, to those who have withstood the risk of hydrocephalus and meningitis, and whose neurological state makes further surgery worth while. Such a policy has obvious appeal to practising surgeons and to many parents. No one likes to contemplate the frightening disabilities to which some of these children are subject, or to operate needlessly on a baby who will surely die. Some patients, indeed, will succumb whatever treatment is offered. In other cases, by a delay of some weeks or months, the parents may be given a much fuller appreciation of the exact neurological disabilities, and the possible benefits of operation can be discussed with them in the light of these disabilities.

On the other hand, the follow-up study of late cases in which this policy has been pursued has revealed that in many cases the parents lost interest in, or were ignorant of, the best welfare of the child. The expected death did not occur, and the practical outcome was that the child was not brought along for treatment of other features of the disability. Consequently, hydrocephalus had progressed to an uncompensated and untreatable degree with consequent brain damage, foot deformities and hip flexures had progressed into contractures, and, in the worst type of case, a severely disabled child crippled in a wheelchair and given no education resulted.

In other words, when the child has survived, it has survived with greater disability that it need have had.

A further disadvantage of delayed operation is the risk of meningitis in patients with ulcerated myelomeningoceles. It has already been pointed out that the risk of meningitis in this series was 35%, and that there was a definite prophylactic value in early operative closure of the lesion in reducing this risk. It is stressed again that the real fear of meningitis is not that the child will die, but that he will survive with more neurological damage and aggravation of his hydrocephalic state than he need otherwise have.

Finally, in deferring operation there are the nursing problems associated with an ulcerated back. There is not only the constant burden of sterile dressings to the back, but to the lay mind of the parents at home, this is viewed with alarm and anxiety. Surgeons often under-estimate this feeling. The parents fear imminent rupture of the horrible mass. Their preoccupation with the infant's care could be all-consuming or, on the contrary, they may be neglectful and meningitis may occur. The preoccupation with the back is a great burden, and places emphasis on the wrong aspects of the disability.

Immediate Opération.

There are several sound arguments for immediate operation.

1. The optimum protection against meningitis is offered. In frankly ruptured masses with deflation of the sac, early operation is practically essential if meningitis is to be prevented.

2. When the back lesion has been satisfactorily dealt with, treatment can be given promptly to other aspects of the disability—feet, hips, bladder, bowel, etc. The parents feel interested, and both parents and surgeons have a joint responsibility from the beginning. Those who survive do so with the minimum disability consistent with the degree of neurological destruction.

3. The parents are relieved from the constant burden of dressings to the back. They can forget the back itself and concentrate on other problems.

It is true that some myelomeningoceles are relatively easy to close by a simple surgical technique in the first few days of life. However, a number of myelomeningoceles are technically inoperable without rather elaborate plastic flaps in order to obtain skin cover, because there may be insufficient sound skin for simple primary closure. It is doubtful whether it is justifiable to embark on the use of complicated pedicle flaps until the baby can prove that survival is worth while. There is an especially good reason for deferring such surgery if the sac is tense and bulging from transmitted hydrocephalus. Otherwise, a post-operative cerebro-spinal fluid leakage with high risk of meningitis is to be expected. Wound breakdown is a serious complication, because, in this series, post-operative leakage with meningitis was nearly always fatal. Surgery should at least be deferred until the hydrocephalus has been controlled, or both aspects should be treated at the same time.

The most serious objection to immediate operation, however, is the question of assessing the severity of the hydrocephalus. It has already been pointed out that 77% of patients in this series developed hydrocephalus, and of these, four out of five died—that is, over 50% of the total number of patients who presented have died from progressive hydrocephalus. Some would hold that the answer to this is a more vigorous approach to the treatment of hydrocephalus, especially since the advent of *ventriculo-atrial shunts*. In these operations there is a relatively simple operative procedure with a mechanical answer to the problem of hydrocephalus. However, I have been impressed by the fact that in many overseas centres a real assessment of hydrocephalus has not been performed, and a valve is simply inserted when the problem arises, often with very little selection of cases. Two dangers seem to be involved in such a policy: (i) The routine early use of a valve shunt shortly after birth can solve the mechanical obstruction to the cerebro-spinal fluid flow, but a number of operations will be needless; either the patient will die in any case, or worse, a surgical success may be achieved on a child with a cerebral cortex of doubtful value. (ii) As one in five patients with hydrocephalus will compensate and their condition will become stabilized without operation (25 out of the 56 survivors),

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There are several sound arguments for immediate operation.

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The most serious objection to immediate operation, however, is the question of assessing the severity of the hydrocephalus. It has already been pointed out that 77% of patients in this series developed hydrocephalus, and of these, four out of five died—that is, over 50% of the total number of patients who presented have died from progressive hydrocephalus. Some would hold that the answer to this is a more vigorous approach to the treatment of hydrocephalus, especially since the advent of ventriculo-atrial shunts. In these operations there is a relatively simple operative procedure with a mechanical answer to the problem of hydrocephalus. However, I have been impressed by the fact that in many overseas centres a real assessment of hydrocephalus has not been performed, and a valve is simply inserted when the problem arises, often with very little selection of cases. Two dangers seem to be involved in such a policy: (i) The routine early use of a valve shunt shortly after birth can solve the mechanical obstruction to the cerebro-spinal fluid flow, but a number of operations will be needless; either the patient will die in any case, or worse, a surgical success may be achieved on a child with a cerebral cortex of doubtful value. (ii) As one in five patients with hydrocephalus will compensate and their condition will become stabilized without operation (25 out of the 56 survivors),

routine early operation for hydrocephalus is therefore unnecessary in some cases.

In other words, there must be a place for more careful selection from the point of view of hydrocephalus before one embarks on needless surgery to the back. The degree of hydrocephalus is difficult to estimate at any time, and is certainly not revealed by a single examination at birth.

The Intermediate Position.

From an analysis of these two points of view, a compromise position has been suggested of waiting five to six weeks after birth as the optimum time to make a decision about the back operation. The reasons are as follows.

1. By this period there is a fuller knowledge of the rapidity and progress of hydrocephalus. There has been a month's observations of serial head measurements and of the clinical state of the child and his potential usefulness, and there has been time to correlate these observations with the results of proper ventriculographic and dye tests. Considerable selection can now be advised regarding operation. In some cases, operation on the hydrocephalus may be advised first. In others, the head is found to be compensating and the back can be treated. In other cases again, neither operation on the back nor on the hydrocephalus will be advised. In addition, by the sixth week, over 90% of the infants will have passed the time when the onset of hydrocephalus is to be expected.

2. Epithelialization will have progressed, so that some myelomeningoceles which were previously inoperable can now be dealt with by a simple operative closure.

3. By such reasonably early operation, the burden of dressings to the back is minimized. The mother is home for two or three weeks after her hospital stay, and the child can be kept in hospital for this period. By the end of the second month the child can be sent home with a healed, flat back. By such early treatment, management can be directed to the other aspects of the disability—the bladder, talipes, etc.—and thus the interest of the parent and of the surgeon alike is maintained from the beginning.

In this interim period of five to six weeks, treatment of the back consists of the application of sterile dressings—a "doughnut" type dressing of cotton-wool—and frequent checking for rupture and infection in the sac, but no parenteral administration of antibiotics is advised. Some myelomeningoceles may still not be ready for operation at this stage, but at six weeks a programme can definitely be mapped out; even if operation is not offered, other features of the disability can be treated and the parents given as much supporting help as possible.

The only indications for immediate operation would seem to be: (i) Frank rupture with deflation of the sac, since the risk of meningitis in such a situation is very high indeed. However, in some of these patients the presence of hydrocephalus at birth will probably decide that no treatment is preferable. (ii) The child who has a myelomeningocele with minimal neurological defects, and in whom simple surgical closure is possible. This child is worth protecting against every risk, including meningitis.

It is stressed that no mention is made in this paper of the multitude of other features in management. More than any specific detail, it is urged that these children need to be under the care of a coordinated rehabilitation team involving close cooperation between many different members—neurosurgeon, orthopædist, urologist, pædiatrician, almoner, physiotherapist and educationist. Although the first few years may be spent in more direct surgical procedures, there must be ever in mind the final rehabilitation to an independent life in open employment. Parents, physician and the child himself must look to this point if the complexities of therapy are not to be overwhelming.

Conclusions.

1. The pathogenesis of myelomeningocele is unknown, but several types of dysplasia must be taken into consideration.

2. A study of the pathology and natural history suggests a policy of advising early operation, but not so early as to be unselective; in particular, to allow some time for full assessment of the hydrocephalic state.

3. It is stressed that long-term planning in a coordinated team approach is required if the complexities of therapy are not to be overwhelming.

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EXPERIENCES WITH ACTINOMYCIN D IN THE TREATMENT OF MALIGNANT DISEASE IN CHILDREN.[1]

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IN children aged five years and over, malignant disease has now become the greatest single cause of death, apart from trauma, and it is one of the major causes of death before the age of five years. Hitherto the burden of striving to do something worthwhile for the unfortunate child with a malignant tumour has had to be shouldered entirely by the surgeon and the radiotherapist. Recent developments in chemotherapy are now providing the physician also with the chance of becoming an active member of the team, with a positive approach to the elimination of the disease.

The primary purpose of this paper is to present a preliminary report on experiences with the use of actinomycin D; but it has been suggested that, as the opening speaker in this session on chemotherapy, I should offer some more general observations as an introduction to the main subject. For this purpose, recent experience at the Royal Children's Hospital will be quoted.

Experience with Cancer Chemotherapy in Children.

In the last 18 months, 29 children with malignant disorders have been referred for consultation with a view to chemotherapy. They received a total of 47 courses of chemotherapy, of which 20 were with actinomycin D (Table I). The earlier cases were all examples of neoplasms with metastases, chiefly Wilms's tumour. However, in the past year a very significant trend has developed; of the last 24 patients referred for chemotherapy, no less than 14 were without clinical or radiological evidence of metastases at the time.

Of these 29 patients, 13 had Wilms's tumour—four without and nine with metastases at the time of chemotherapy. The important role of actinomycin D in their treatment is referred to later. Two patients were treated at a time when supplies of actinomycin D were temporarily unobtainable. Instead they were given "Nitromin", an oxide of nitrogen mustard introduced by the Japanese. Though extremely useful for malignant lymphoma and certain other tumours, it proved of very limited value in these two cases of Wilms's tumour. The one course of steroid therapy was given to a boy in the terminal stage; he derived symptomatic benefit, albeit without significant regression of the tumour masses.

For neuroblastoma a wide range of drugs has been found to produce in some cases clinical remission and regression of the tumour. These include the cytotoxic drugs, nitrogen mustard and other alkylating agents of related chemical structure; the antimetabolites, aminopterin, "Methotrexate" (amethopterin) and 6-mercaptopurine; the steroids; vitamin B_{12}; and now actinomycin D.

[1] Read at a meeting of the Australian Pædiatric Association, Canberra, April 22 to 25, 1960.

[2] Working with the assistance of a grant from the Anti-Cancer Council of Victoria.

TABLE I.

Number of Cancer Patients Treated by Chemotherapy, 1958 to 1960.

Type of Malignant Disease.	Number of Cases.	Number of Courses Given.				
		Actinomycin D.	Nitromin.	Steroid.	Aminopterin.	Other.
Wilms's tumour	13	13	2	1	—	—
Neuroblastoma	4	2	1	1	1	—
Osteogenic sarcoma	3	2	1	—	—	Mitomycin C, 2.
Rhabdomyosarcoma ..	2	2	1	1	—	—
Lymphosarcoma	2	—	—	1	2	"Leukeran" (chlorambucil), 2.
Miscellaneous[1]	5	1	5	4	—	Vitamin B_{12}, 1. Triethylene melamine, 1.
Total	29	20	10	8	3	6

[1] Includes retinoblastoma, embryonal carcinoma in teratoma, possible adenocarcinoma of liver, Hodgkin's disease and eosinophilic granuloma of bone, one case of each.

Their effectiveness was well tested on one of our patients, a boy, aged four years, with a large, diffuse, hæmorrhagic and almost inoperable thoracic neuroblastoma. After partial surgical excision, radiotherapy and vitamin B_{12} therapy he improved, but nine months after operation there was radiological evidence of pulmonary metastases. Since then he has had a thoracotomy, "Nitromin" (two courses), prednisolone and recently actinomycin D, and at the moment he feels and looks well three years after the onset of his symptoms.

Another child, who has perhaps wrongly been listed in Table I under the "miscellaneous" group as having a possible adenocarcinoma of the liver, is considered by an overseas pathologist as more probably having a neuroblastoma with hepatic metastases. She presented at the age of three months with a truly enormous liver, from which a biopsy was taken at laparotomy. With vitamin B_{12} as the only treatment, her liver has been slowly regressing in size, and she is at present symptomless at the age of nine months

On the whole, however, our results with vitamin B_{12} for neuroblastoma have not confirmed the claims of Bodian (Bodian, 1959).

Of our three patients with osteogenic sarcoma, one received actinomycin D in a late stage of metastases, with temporary benefit. Two were treated with mitomycin by local perfusion, and these will be reported on by others in due course.

Rhabdomyosarcoma is a tumour that is commonly insensitive to irradiation alone, but reports indicate that prior treatment with actinomycin D may make the tumour radiosensitive. Our experience with one enormous tumour so treated provided little evidence of this. The other tumour originally suspected of being a rhabdomyosarcoma subsequently proved to be an undifferentiated sarcoma of the prostate. Actinomycin D was given only three months before death, with little benefit to the patient.

Lymphosarcoma, along with other malignant lymphomas, will respond for a variable time, that may sometimes run into years, to several types of drug. The most useful of these seem to be the alkylating agents of the mustard group, the folic acid antagonists and actinomycin D, with steroids to assist in emergencies. We have tried all these. The natural course of these tumours is so variable that no conclusions can yet be drawn, but one case seemed to indicate the potency of chemotherapy.

A girl, aged four years, with advanced Hodgkin's disease, was flown home from a mission station in India with a history of symptoms of eight months' duration. By this time she was in the third stage, with enlargement of the liver, spleen and lymph glands, with bone-marrow involvement and severe pancytopenia in the blood, and with extensive infiltration of the lungs. After two weeks' treatment with prednisolone, there was a remarkable improvement in her clinical condition and in the radiological picture of the chest. With the addition of "Nitromin", the pulmonary lesions cleared almost completely, and it was eight months before there was any sign of a relapse.

Other malignant diseases of childhood for which chemotherapy has been found to be of some value include various sarcomas, testicular tumours, embryonal carcinoma, retinoblastoma and leukæmia. Eosinophilic granuloma has been included in Table I because it sometimes proves to be a malignant condition, although it is not a neoplasm. In this one case, in which a very large granuloma of the ilium was present, surgery and radiotherapy were contraindicated and steroid therapy proved ineffective, but a ten weeks' course of "Nitromin" produced a very striking response, which to date has persisted for 12 months.

This brief and sketchy survey of some of the uses of chemotherapeutic agents for pædiatric malignant disease is all that time will permit. It is sufficient both to indicate that there is a rapidly widening scope for chemotherapy in addition to surgery and radiotherapy, and to provide a background for the description of the use of actinomycin D which follows.

TABLE II.

Incidence of Toxic Effects of Actinomycin D in Relation to Dosage.

Course Dosage. (Micrograms per Kilogram.)	Number of Courses.	Toxic Effects (Number of Cases).						
		Cellulitis.	Anorexia.	Vomiting.	Stomatitis.	Alopecia.	Thrombocytopenia.	Neutropenia.
60 to 89	6	4	1	1	—	—	—	—
90 to 119	8	3	6[1]	7[1]	1	1	1[1]	2[2]
120 to 149	4	—	3[2]	2[3]	—	1	2[2]	2[2]
150 to 180	4	1	3	2	2	3	2	1
Total	22	8	13[4]	12[4]	3	5	5	5

[1] In three with fever.
[2] Developed only during subsequent deep X-ray therapy.
[3] In one with fever.
[4] In four with fever.

Use of Actinomycin D.

The actinomycins are a group of antibiotics obtained from the culture of various species of the genus *Streptomyces*. They are unique in being composed of a polypeptide grouping attached to a phenoxazone chromophore, and they differ from each other in the amino acid content of the peptide grouping. They proved to be too toxic for use as anti-infection agents, but Farber, at the Children's Cancer Research Foundation in Boston, found that actinomycin D would inhibit the growth of transplantable tumours and leukæmia in mice (Farber, 1955). Clinical trials followed, showing that this substance would produce some benefit in cases of rhabdomyosarcoma, Wilms's tumour and Hodgkin's disease, but that it was ineffective in the acute leukæmia of childhood (Farber *et alii*, 1956). In the following year, Charlotte Tan *et alii* (1957), from the Memorial Center for Cancer and Allied Diseases in New York, and Aquirre and Sosa (1958), from Mexico, presented the results of actinomycin D therapy in a total of 57 children with disseminated neoplasms; they found improvement in a high proportion of cases of Wilms's tumour, malignant lymphoma and neuroblastoma. Since the commencement of the present study, these earlier favourable reports have been confirmed by several further papers (Pinkel, 1959; Tan *et alii*, 1959; Farber *et alii*, 1960).

We first used actinomycin D in November, 1958, for the child with Hodgkin's disease already discussed, and then, through the courtesy of Mr. Douglas Stephens, an opportunity arose to use it for a child with pulmonary metastases from a Wilms's tumour. The results in this case were so striking that we were encouraged to continue the trial in a steadily widening range of malignant conditions. Up till the end of March, 1960, a total of 22 courses of this substance had been given to 20 patients, two of them receiving a second course.

Actinomycin D is now supplied in sterile solution in a concentration of 0·5 μg. per millilitre. It has to be administered intravenously. This does provide a certain hazard to small infants, because the substance is extremely irritating to soft tissues, and extravasation outside the vein is likely to lead to non-suppurative cellulitis and to thrombosis in the vein. In small infants we therefore make the maximum use of the intravenous drip method, and in the absence of this it is often advisable to use the "two-needle technique" when the drug is administered directly into a vein. In eight of our 20 cases, chemical cellulitis with venous thrombosis developed at the site of injection, and seven of these patients were aged under two years. Actual ulceration occurred in three of them; it healed completely, but only after several weeks. Oral administration as an alternative has been discarded overseas because of the severity of the toxic effects on the gastrointestinal tract.

Dosage and Toxic Effects.

Pinkel (1958*a*, *b*) maintains that body surface area is better than body weight as a criterion for the estimation of dosages, and that the optimal dosage of actinomycin D for children is 2·4 mg. per square metre of body surface area. However, body weight has been taken as the basis for estimations in most centres, the dosage usually being 10 to 15 μg. per kilogram, repeated daily for five to seven days. This gives a total dosage for the course of about 60 to 100 μg. per kilogram. In our hospital for diverse reasons, some of them beyond our control, we have experimented somewhat in the matter of dosage. The total dosages per kilogram have ranged from 60 to more than 180 μg. for a course. Rightly or wrongly, we have assumed that the optimal dosage of an anti-cancer drug must be the maximum that the patient can reasonably tolerate, and so we have watched particularly closely for the signs of toxic effects. Our experience to date gives the impression that the optimal dosage for a course spread over seven to ten days is between 100 and 120 μg. per kilogram, though some infants may tolerate more than this. The timing of a course of radiotherapy has some bearing on the dosage of actinomycin D that can be tolerated. We do not at present administer these two forms of therapy simultaneously, as is the practice in at least some centres overseas.

The principal toxic effects of actinomycin D can be grouped under four headings: (i) those involving the alimentary tract—anorexia, nausea, vomiting, diarrhœa, ulcerative stomatitis; (ii) dermatological effects—alopecia and occasional skin eruptions (erythema at sites of previous radiotherapy, acne, etc.); (iii) hæmatological effects—thrombocytopenia, neutropenia and occasionally anæmia; (iv) local irritation causing non-suppurative cellulitis at the site of injection. Of these manifestations, nausea, vomiting and diarrhœa may occur on the day of injection, but the more serious effects such as stomatitis, alopecia and hæmatological complications are apt to occur during the week following the end of a course.

The incidence of these toxic effects and their relationship to the dosage used in the 22 courses in this study are shown in Table II. As was to be expected, the greater the total dosage, the greater was the incidence of the more serious manifestations of toxicity. At first sight this list of apparent toxic effects encountered in the study looks rather forbidding; with only four courses were none at all recorded. But the true picture is much brighter than this. Of the 13 instances of anorexia and/or vomiting, four were due almost certainly to concurrent febrile infections, and two were considered on good grounds to be the result of emotional factors. In only two of the remaining seven cases was the vomiting severe in degree, and the total dosage of actinomycin D in each of these two would now be considered excessive—that is, over 150 μg. per kilogram. Stomatitis and alopecia likewise were of only minor degree, except in patients who had received excessive dosages. Of the five examples of hæmatological depression, three occurred only four to six weeks after the chemotherapy, during a course of irradiation which can be considered at least partly responsible, and the two other examples followed excessively high dosage of the drug. Furthermore, in all cases the toxic effects, however severe, proved to be reversible with treatment, complete recovery occurring as a rule within two to three weeks, or a little longer in the case of alopecia.

Thus we consider now that with good intravenous injection technique, with the avoidance of a total dosage as high as 150 μg. per kilogram of body weight, and with good collaboration with the radiotherapist, severe toxic reactions become the exception, and that, as they are reversible, they are not too high a price to pay for successful treatment of a malignant condition.

Therapeutic Results.

Just how successful are the results of treatment with actinomycin D? Their complete assessment will require a prolonged follow-up period, probably of five years. We cannot report on this basis for some time, and even in America it is only just becoming possible with the handful of patients who received actinomycin D in 1954-1955. Survival curves and two-year follow-up studies must be the basis of reports that were presented only a fortnight ago in New York and Chicago. To Dr. Arthur Clark and Dr. Basil Stoll I am indebted for summaries of these recent reports. In brief, they indicate that either actinomycin D or actinomycin F, when given alone, will produce tumour regression in at least 70% of cases of Wilms's tumour, in at least 40% of cases of neuroblastoma and in at least 20% of cases of rhabdomyosarcoma. Surgical excision and radiotherapy may further improve the prognosis. At the Children's Cancer Research Foundation in Boston, approximately half the patients with Wilms's tumour now survive for at least two years—and these results appear to have been obtained with dosages of actinomycin D that are 25% to 50% lower than we have recently come to adopt in our hospital.

It is too early as yet for us to draw any valid conclusions regarding the effect of chemotherapy on the

survival of our own patients, although in some cases the impression gained is certainly favourable. We have, however, through the commendable enthusiasm of our surgeons, been able to make some enlightening observations on the microscopic pathological features of lesions from which biopsies were taken after chemotherapy. On three children with pulmonary metastases from Wilms's tumour, lobectomy was performed by Mr. Russell Howard between one and eight months after a course of actinomycin D. Dr. Alan Williams, the Director of Pathology, found in the metastatic nodules in each case a most encouraging reversion towards a normal histological picture.

The first of these three patients was a girl, aged five and a half years when Mr. Douglas Stephens performed a nephrectomy for Wilms's tumour; this was followed by deep X-ray therapy. The chest was known to be radiologically clear up to ten months after operation, but after 13 months two metastases were detectable in the upper lobe of the right lung, and they had increased in size three months later. At this stage, in November, 1958, a course of actinomycin D totalling about 90 μg. per kilogram of body weight was given. Sixteen days later one of the metastatic nodules was no longer visible in the X-ray film, and there was only a faint shadow at the site of the other one. Six months later this second nodule seemed to be enlarging again. A second course of actinomycin D was then given, but the radiological picture had not altered a month after this course. Mr. Russell Howard therefore removed the upper lobe of the right lung. At the present moment this girl is well and free from any signs of metastases ten months after lobectomy, 17 months after her first course of actinomycin D and nearly three years after her nephrectomy.

It was certainly impressive that in the biopsy specimens from this case and from the two other cases in which lobectomy was performed subsequent to actinomycin D therapy, Dr. Alan Williams reported finding a histological picture virtually devoid of malignant cells and containing elements of fibrous tissue, striated and non-striated muscle and renal structures far more mature than had been found in the original tumour.

It can be concluded, from our limited experience to date, that actinomycin D will produce results, for Wilms's tumour at least, that we were not able to obtain in previous years with surgery plus radiotherapy. It may yet prove possible to enhance the effectiveness of this substance by varying the dosage and schedule of administration. Longer follow-up studies may also produce definite evidence of improvement in survival curves and cure rates. Finally, it seems justifiable to extend the trial of actinomycin D to cover a wider range of pædiatric malignant disorders.

Summary.

1. A brief general survey of chemotherapy for malignant disease has been presented, to indicate that this form of treatment merits consideration in most cases of cancer in childhood.

2. By culling the previous clinical reports of acinomycin D and describing our experiences of its administration, dosage and toxic effects in 22 instances, it has been shown that this substance is highly toxic, but that it can be safely used if appropriate precautions are taken.

3. Therapeutically, actinomycin D has been shown to produce a striking beneficial effect on the microscopic as well as on the macroscopic picture of Wilms's tumour.

Acknowledgements.

It is a pleasure to acknowledge that the opportunity of carrying out these trials of actinomycin D has been due to the wholehearted cooperation and encouragement of my surgical colleagues, Mr. Russell Howard, Mr. Murray Clarke, Mr. Douglas Stephens, Mr. N. A. Myers and Mr. Peter Jones, and that the results recorded with Wilms's tumour have been obtained in collaboration with them. I am also indebted to the Honorary Radiotherapist, Dr. G. R. Kurrle, of the Peter MacCallum Clinic, for considerable advice, to Dr. Alan Williams, the Director of Pathology, and to Dr. H. G. Hiller, the Director of Radiology, for diagnostic assistance, and to many of my medical colleagues for their cooperation and helpful criticism. The supplies of acintomycin D were kindly made available for this study by Merck, Sharp and Dohme, initially through the Peter MacCallum Clinic.

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MASSIVE CHEMOTHERAPY IN MALIGNANT DISEASE IN CHILDHOOD.[1]

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AN increasing number of chemical agents are beginning to play their part in the attack against malignant disease. This is particularly so in the pædiatric age group, since many of the malignant conditions that we see in children either are truly multicentric in their origin, or advance so rapidly that they are already beyond the scope of surgery or radiotherapy when the child is first seen. Unfortunately, the antimitotic effect of the drugs at present used is not confined to cancer cells. Any cells in the state of active division appear to be peculiarly susceptible to their effects. The concentration of a cytolethal agent which will inhibit the multiplication of cancer cells would also affect the cells of the gastro-intestinal tract and, even more important, those of the bone marrow. This fact has hitherto precluded us from employing really high dosages of these drugs in our attack against cancer, and therefore their use has been largely palliative. However, Creech and his co-workers have recently shown that it is anatomically feasible to isolate a part of the body and to direct into this portion a large dose of a suitable cytolethal agent, while the remainder of the body, and in particular the bone barrow, is protected from the effects of this drug.

The work of Creech and his associates has largely been directed against malignant melanomas and a number of sarcomas and carcinomas, mainly in adult patients. It has always seemed to us that chemotherapy is peculiarly applicable to the cancers of childhood. It has been known for some time that many of the malignant tumours seen in childhood are particularly susceptible not only to radiation therapy but to various cytolethal agents, and since malignant disease is unhappily frequently seen in a disseminated from in the pædiatric age group, in many cases some form of chemotherapy is the only form of treatment that can be considered.

It is emphasized that this paper is intended only as a preliminary report, since only a very few patients have been treated, and none of these for long enough to give

[1] Read at a meeting of the Australian Pædiatric Association, Canberra, April 22 to 25, 1960.

any reliable opinion as to the long-term effects of this form of therapy. However, certain techniques have been worked out for the administration of large amounts of these drugs without adverse effects on either the bone marrow or the gastro-intestinal mucosa, and the purpose of this paper is to set out these techniques in the hope that they may be utilized in a reasonably uniform manner throughout the various pædiatric institutions in Australia, so that at some future date our combined results may be collected and analysed and again presented. In this way, sufficient experience may be accumulated relatively quickly in order to enable us to evaluate this form of treatment of malignant disease in childhood.

The following is the recommended total-body dosage for superdosage chemotherapy in malignant disease (these figures represent the LD_{05} for Rhesus monkeys):

Nitrogen mustard	1·1 to 1·4 mg. per kilogram
Nitromin	25 to 28 mg. per kilogram
T.E.M.	15 to 18 mg. per kilogram
Thiotepa	1·3 to 1·5 mg. per kilogram
Actinomycin D	50 µg. per kilogram
Mitomycin C	1·2 to 1·5 mg. per kilogram

The drugs are all administered intravenously as a single dose.

As these figures represent the LD_{05} for Rhesus monkeys, they are therefore probably reliable for humans. Originally the marrow was protected by isolating one leg and freezing it to 15° C., removing marrow from the iliac crest and injecting this into the tibial marrow cavity of the isolated leg. Isolation was continued for a period of three to four hours, after which the tourniquet which had been placed around the thigh was released and circulation in the leg was reestablished. This limited the cytolethal agents available to short-acting drugs such as nitrogen mustard, which would quickly be fixed by the tissues, so that at the end of three to four hours an insignificant amount remained circulating in the blood to affect the marrow stored in the isolated tibia. In addition, it was thought that there were real dangers to the isolated limb, and in some instances necrosis of skin underlying the tourniquet occurred. It was therefore decided to store the withdrawn marrow in a suitable solution and to replace it after an interval of 12 to 24 hours. Discussion with the Red Cross Blood Transfusion Service and a survey of the literature indicated that a multi-electrolyte preparation, known as Hanks' solution, combined with heparin and serum albumin should prove to be a suitable vehicle. The formula for Hanks' solution is as follows:

Sodium chloride	8·0 grammes
Potassium chloride	0·4 gramme
Magnesium sulphate	0·2 gramme
Calcium chloride	0·14 gramme
Sodium phosphate	0·06 gramme
Potassium phosphate	0·06 gramme
Glucose	2·0 grammes
Distilled water to 1 litre	

The pH is adjusted to 7·6 with 0·3N sodium hydroxide solution. The solution used for storage of the marrow is as follows: Hanks' solution 80 ml., albumin (25%) 20 ml., heparin 500 units. Twenty to 50 ml. of marrow are removed from the iliac crests into syringes of 20 ml. capacity containing 10 ml. of the storage solution. This marrow mixture is placed in a suitable container and stored at 4° C. until required for replacement.

A minimum of 20 ml., and preferably 30 to 50 ml., of marrow is withdrawn from the iliac crest, 10 ml. at a time, using a marrow aspiration needle with a syringe containing an equal quantity of the special solution. The marrow suspension is then stored in a refrigerator at 4° C. for 12 to 24 hours, after which the child is given another short anæsthetic and the marrow mixture is replaced into the iliac crest. After operation the patient is given tetracycline (50 mg. per kilogram), cortisone (25 to 50 mg. twice a day), folic acid (5 to 10 mg. per day) and vitamin B_{12} (500 to 1000 µg. every second day).

The advantages of this technique are obvious. First, there is no danger to any limb, and secondly, a much wider variety of cytolethal agents are available for use, since the choice need not be confined to short-acting drugs. In the limited number of instances in which this technique has been used, no permanent evidence of marrow depression has resulted. Occasionally temporary neutropenia or pancytopenia will occur towards the end of the first week, only to disappear in the ensuing week as marrow regeneration occurs.

Limb and Organ Perfusion.

Creech has used the technique of local perfusion for the limbs, the breast, the lungs and the pelvis. Our limited experience has so far been confined to the lower limbs and upper limbs. In the case of the lower limb, the main vessels are exposed and cannulated, a larger cannula being used in the vein than in the artery whenever possible. Gravity drainage from the vein into the heart-lung circuit is utilized, the only pump in the circuit being that which is used to return the blood to the femoral artery. A tourniquet, although recommended by Creech, is not used, and does not seem to make any significant difference to the amount of spill-over into the general circulation which occurs. It is convenient to tag the cells of the perfusate with radio-chromium, and subsequently to determine the amount of spill-over that has occurred. In the absence of a tourniquet, as a precautionary measure marrow is aspirated from the iliac crest prior to perfusion and suspended in the modified Hanks' solution, and if subsequent tests indicate a significant degree of spill-over, then the marrow can be replaced 24 hours later.

With regard to the dosages of drugs utilized, we have in general followed Creech's recommendations as to both total amount and method of administration, and these figures are set out for convenience in Table I.

TABLE I.

Recommended Dosages for Limb and Organ Perfusion.

Cytolethal Agent.	Dose per Kilogram of Body Weight.		
	Pelvis.	Lower Limbs.	Upper Limbs.
Nitrogen mustard	1 mg.	0·8 mg.	0·6 mg.
Phenylalanine mustard	2 mg.	1·5 mg.	1·5 mg.
Actinomycin D	50 µg.	50 µg.	35 µg.
Mitomycin C	1 mg.	1 mg.	0·8 mg.

The drugs are given in three equal divided doses five minutes apart, and perfused for a total of 30 minutes from the administration of the initial dose. With the exception of nitrogen mustard, the residual drug is removed by flushing the limb through with 500 ml. of "Dextran", infused through the arterial cannula and drained from the venous line.

The pump used is of the simple occlusive De Bakey type, and it is important that it should be able to run slowly enough to deliver the very small volume flow required in young children. The total body flow requirements are worked out on the basis of 2·4 litres per square metre of body surface (70 to 100 ml. per kilogram per minute), and the flow for any particular limb is assessed as follows: pelvis, one-sixth of total body flow; lower limb, one-eighth of total body flow; upper limb, one-twelfth of total body flow.

A simple disposable plastic oxygenator known as a "Pulmo-Pak", manufactured by Abbott Laboratories, seems ideally suited for this particular use, since it requires only a small amount of blood for priming and it is completely disposable. The smallest possible volume of blood should be used for priming, in order to obtain the maximum concentration of drug in the perfusate and the maximum number of circulations of the drug during the

time available. In general, 1 litre of blood will be found adequate for priming the circuit. Heparinized blood is, of course, used, and this can, if more convenient, be collected the day before. The set-up used is shown diagrammatically in Figure I.

The "Pulmo-Pak" should preferably be on an adjustable arm, so that the level of the reservoir in relation to the femoral vein may be altered according to needs. The height of the blood level in the reservoir should initially be 10 in. below the level of the femoral vein. Immediately prior to cannulation of the main vessels, a dose of heparin (2 mg. per kilogram of body weight) is given. This is subsequently neutralized with polybrene in a milligramme for milligramme dosage, or with protamine (1·5 mg. per milligramme of heparin). In the case of the upper limb the technical difficulties are

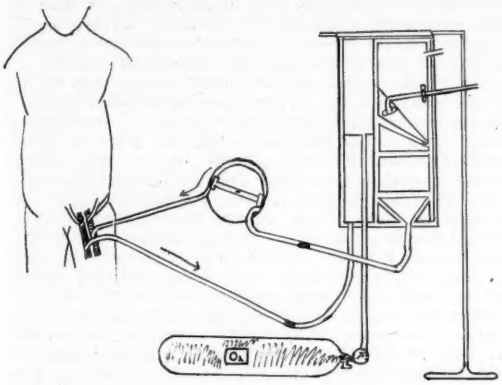

FIGURE I.

greater. Although the axillary artery is adequate for perfusion, it will not infrequently be found that the axillary vein is too small to give an adequate venous return, so that in children it will probably be wise to use the subclavian vessels for perfusion of the upper limb. A certain amount of spill-over of the perfusate into the general circulation is regarded as desirable, since it is thought that the presence of a proportion of the cytolethal drug in the general circulation may inhibit the subsequent appearance of metastases. Up to 25% of the total drug injected as a spill-over is probably acceptable and even desirable, and even up to 50% would probably still be within the margin of safety, if the dosages recommended are adhered to. No general or local ill-effects of any consequence have been seen as a result of perfusion in the limited number of cases so far dealt with. However, it is once again emphasized that this is very much in the nature of a preliminary report, to communicate the techniques that have been developed in the hope that work along similar lines will be stimulated in the other pædiatric centres in Australia.

Report of a Case.

A female patient, aged 11 years, was first examined in May, 1959, when she complained of an ache in the right leg present off and on for six months, and worse for the last two weeks. Swelling of the lower third of the right thigh had been noted for three days. There was no history of injury. The pain now awakened her at night.

On examination of the patient, there was a hard, tender swelling in the lower third of the right femur, and X-ray examination revealed an obviously malignant bone tumour. Opinions were divided, both here and in Boston, as to whether this was a Ewing's tumour or an osteogenic sarcoma. Radiation therapy was commenced and continued to a total tumour dose of 6000*r*, during which time the tumour progressed rapidly and appeared to be quite unaffected by radiation.

Limb perfusion with mitomycin C was carried out on July 16, 1959. Since that time there has been no evidence of progression in the local tumour; in fact, it appears to be significantly smaller clinically, although the X-ray appearance has been virtually unchanged. The lungs were clear at this stage, but several secondary growths became obvious in August, 1959. However, these have shown no further progress, and no further secondary deposits have become evident.

The child is very well, having gained more than a stone in weight since November. She is walking on crutches and taking a limited amount of weight on the right leg. Her further progress will, of course, be followed with considerable interest.[1]

Conclusion.

In conclusion, I feel that we must reorientate our thinking with regard to cancer in childhood, which tends to be conditioned by the progressive nature of malignant disease as seen in adults.

In childhood, cancer is in many instances a disease of potential remissions and exacerbations, and every effort should be made to achieve the former. It should always be remembered that we are dealing with a family group rather than with a single patient, who must all be protected as far as possible from an extremely traumatic experience. The magic of hope should almost never be withdrawn from the family, and even when any chance of long-term survival is remote, palliation is almost always warranted for this reason alone, and to give the parents sufficient time to adjust themselves to the situation that has arisen.

Acknowledgement.

Dr. Albert Freedman, of the Special Unit for Malignant Disease in Sydney, has provided the figures for the recommended total-body dosage of the various drugs used. I am indebted to him for much helpful advice relating to the use of chemotherapy in all cases we have treated.

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THE INCIDENCE OF INFECTIONS FOLLOWING SPLENECTOMY IN CHILDHOOD.[2]

By MARGARET HORAN, M.R.C.P., M.R.A.C.P.,
Royal Children's Hospital, Melbourne.

KING AND SCHUMACKER, in 1952, were the first to draw attention to serious infections following splenectomy in infants aged under six months at the time of operation. Since then, there have been numerous similar reports of meningitis, septicæmia and other serious infections following splenectomy in children of all ages; but in all these reports the data are insufficient for a true assessment of the incidence to be made. The present survey was undertaken to determine whether the underlying disease and the age at the time of splenectomy do affect the incidence of infection.

In the 20 years from 1938 to 1958, splenectomy was performed at the Royal Children's Hospital and the Queen Victoria Memorial Hospital, Melbourne, on 142 children aged from 14 weeks to 16 years. Of these children 135 came under review and six could not be traced, and in one case follow-up investigation was unsatisfactory. A satisfactory follow-up investigation

[1] In October, 1960, the child was in excellent health and walking without crutches.

[2] A summary of a paper read at a meeting of the Australian Pædiatric Association, Canberra, April 22 to 25, 1960.

required a minimum period of two years since splenectomy and a reliable history, particularly relating to serious infections.

The majority of patients were aged between four and 13 years at the time of splenectomy. Boys outnumbered girls by three to one in cases of trauma, but in other conditions the numbers were roughly equal. There were 61 cases of traumatic rupture of the spleen, 38 of hereditary spherocytosis, three of acquired hæmolytic anæmia, 13 of idiopathic thrombocytopenic purpura, 10 of portal hypertension and four of Cooley's anæmia, and six miscellaneous cases. There were 17 serious infections in 135 children; 10 of these cases occurred within two years of splenectomy. There were two cases of non-fatal meningitis, three cases of fatal septicæmia, seven cases of non-fatal pneumonia, three cases (one fatal) of subphrenic abscess, one case of non-fatal osteomyelitis and one case of fatal tuberculosis. Organisms were cultured in only seven cases—too few to show a correlation between the organism and the disease it produced.

In 61 cases of trauma, there were four serious but non-fatal infections, whereas in 74 children with an underlying disease there were 13 infections with five deaths. This difference is not statistically significant; but it does suggest that the underlying disease may lead to an increase in susceptibility to infection. There were four serious infections, three of them fatal, in nine children aged under six months. This incidence was much higher than in children in the older age groups, and the difference was statistically significant in regard to age. Six of these nine infants were suffering from hereditary spherocytosis and two of these six died.

Conclusion.

Definite answers to the questions raised could not be obtained from these figures alone, or in combination with previously reported material. There are still not sufficient fully documented cases for it to be stated categorically that the underlying disease and removal of the spleen do affect the incidence of serious infections. The fact that four serious infections in infants aged under six months were encountered in 17 cases at all ages strengthens the case for deferring splenectomy, when it is not actually life-saving, beyond the period of infancy.

SOME PROBLEMS CONNECTED WITH CHILDHOOD HEPATIC CIRRHOSIS.[1]

By S. T. ACHAR, M.D., F.R.C.P. (C.),
Director and Professor of Pædiatrics, Institute of Pædiatrics, Madras Medical College, India.

I PROPOSE to take some problems connected with childhood hepatic cirrhosis and try to review the existing position briefly. Rather than report on my own work, I shall try to fit in small fragments into the total over-all picture. Hepatic cirrhosis is seen among children all over the world and in a certain number of instances the cause is indeterminate. There seems to be a greater prevalence of cirrhosis among the children in the tropics and subtropics. However, it is in India and the West Indies, two widely separated regions of the world, that cirrhosis is sufficiently common in children aged between one and five years to constitute a public health problem in those regions. The ætiological factors are not the same in the two regions; toxic alkaloids in the bush teas used as beverages for infants in the West Indies are responsible for the cirrhosis in Jamaican cases, while these or allied toxic substances have not so far been known in the diet or beverages of children in India. A high incidence is also reported among children in the Austrian Tyrol.

[1]Read at a meeting of the Australian Pædiatric Association, Canberra, April 22 to 25, 1960.

The known causes of childhood cirrhosis are many, and may be listed as follows: viral hepatitis, neonatal hepatitis and, rarely, other viral diseases affecting the liver; hepatolenticular degeneration; congenital biliary atresia; rarely, galactosæmia, glycogen storage disease and lipoidosis; muscoviscidosis—but portal hypertension or clinical signs of cirrhosis are not usually present; ulcerative colitis; protein malnutrition (?); congenital syphilis (?); veno-occlusive disease (due to toxic alkaloids); congenital fibrosis of the liver—a rare condition; indeterminate causes (Indian childhood cirrhosis, childhood cirrhosis in the Austrian Tyrol, a percentage of cases all over the world).

When is one to suspect cirrhosis? The well-established cases associated with a hard nodular or granular liver, ascites and other evidences of portal hypertension need no comment. It is the clinically latent cirrhosis or the child with minimal symptoms and slightly enlarged liver which poses diagnostic problems. The liver is normally palpable below the costal margin in infancy and early childhood, but the extent which can be considered to be within normal limits seems to have been worked out in only a few centres. In one study from a well-nourished community, the average projection of liver below the right costal margin in the mid-clavicular line in the end-respiratory position was 1·6 cm. up to the age of 18 months, gradually becoming less, with significant numbers in the older age groups not showing any projection at all. In areas of the world and in communities where the protein consumption is suboptimal among children, it is to be expected that the liver would be slightly enlarged and would project below the costal margin, owing to varying degrees of fat accumulation in the liver, even without any symptoms. Such has been our experience at Madras. The fatty liver has a smooth surface and feels soft and its edge is rounded, while the cirrhotic liver is hard and perhaps granular to the feel, and has a sharp edge.

The clinical features of hepatic dysfunction or hepatocellular failure help to some extent in the diagnosis. Spider nævi are not often seen in younger children with cirrhosis. Hæmatemesis, melæna or the presence of œsophageal varices (often demonstrable by X-ray examination with a barium bolus and by œsophagoscopy) indicate portal hypertension, which may be due to intrahepatic or extrahepatic portal obstruction. A palpable spleen is sometimes the only clinical indication of portal hypertension. Estimation of intrasplenic pressure is useful to assess this hypertension before a decision is made to do shunt operations. This estimation could conveniently be done as a preliminary step while the diagnostic procedure of spleno-portal venography is being undertaken. Biochemical tests as aids in the diagnosis of early cirrhosis are of limited value, because of the vast reserve power in the liver which has been mildly or moderately damaged. In infants aged below six months the results may be negative or borderline despite unequivocal signs of liver dysfunction. Liver biopsy is of diagnostic help in early or doubtful cases and sometimes in assessment and prognosis. There is no need of this procedure for diagnostic purposes when the clinical picture is that of decompensated cirrhosis, or when the liver is definitely hard and granular to the feel. Hepatic-cell necrosis cannot always be made out, but lesser degrees of liver-cell damage, line swelling and ballooning can be striking in these sections. In the present state of knowledge, as Hans Popper put it, we are apparently unable to recognize the existence of hepatic failure from the histological picture because there seems to be no correlation.

The role of protein malnutrition in the pathogenesis of hepatic cirrhosis in the pædiatric age group is not clear, though tacit assumptions have been made in the past because of Himsworth's experimental production of fibrosis in rats by diet alone. In Madras, both protein malnutrition and childhood cirrhosis are common. In an attempt to find out whether protein malnutrition leads to hepatic cirrhosis in the pædiatric age group, we have tried to follow clinically and by serial liver biopsy, children originally

admitted into the hospital with nutritional œdema (kwashiorkor). We were able to follow 36 such patients, two for a period of eight years, 16 for six years and 18 for four years. They all had fat vacuolation in the liver during the period of florid kwashiorkor, some of them had mild portal mesenchymal reaction and two had stellar fibrosis; but none developed cirrhosis during the years of follow-up investigation, though two of them showed septal fibrosis in the liver biopsy sections, one two years and the other three years after discharge from hospital after the kwashiorkor episode. Even this septal fibrosis regressed in later biopsies. Those siblings of these children receiving the same type of protein-deficient diet at home whom we were able to observe did not develop cirrhosis during this follow-up study. A large number of children with Indian childhood cirrhosis (a non-committal term for cirrhosis of indeterminate cause commonly occurring in India in the age group one to five years), whom we were able to study clinically during the past few years in Madras, aided by serial liver biopsies in some cases from the early stage to the well-advanced stage, did not show fat vacuolation in the liver sections at any stage, but showed a histological picture of chronic hepatitis in the liver before the stage of well-established cirrhosis. Also, these cirrhotic children were not from the very poor families from whom most of our kwashiorkor patients come. The diet of the cirrhotic children before they developed cirrhosis was fair in protein intake, though not optimal in some, and was far better than the diet of the kwashiorkor patients. For these reasons, we think that the present evidence does not point to a direct relationship between protein malnutrition and hepatic cirrhosis. However, we have occasionally encountered hepatic fibrosis associated with fat vacuolation in the liver, but not true cirrhosis, in a few children with a poor dietetic history and some evidences of protein malnutrition. Such cases, which occurred in older children, have been far fewer (only 16 in nine years in our clinic) than cases of Indian childhood cirrhosis and chronic hepatitis (over 250 in our clinic in the same period of nine years); the course was benign, all the patients improving remarkably, both clinically and in the histological picture of the liver, with good diet. This leads us to surmise that prolonged protein malnutrition may occasionally give rise to hepatic fibrosis in an older child and perhaps in adult life, but does not seem to be a factor in the causation of the widely prevalent cirrhosis in young children in Madras, known as Indian childhood cirrhosis.

Does reversal of well-formed fibrous tissue ever occur in established cirrhosis? There have been stray instances of such reversal in our series in Madras, as in the following case.

A girl, aged nine years, with post-viral hepatitis and cirrhosis, was admitted to hospital with hepatosplenomegaly, portal hypertension and hæmatemesis. She was operated upon (splenectomy with porto-caval shunt), and is now in good health, the liver not being palpable, four years after operation. Biopsy of the liver at operation showed extensive fibrosis. Repeated liver biopsies, one year and two years after the operation and the patient's restoration to good health and activity, showed hardly any fibrous tissue (Figures I and II).[1] This child had also repeatedly received gamma globulin from pooled adult sera parenterally once in three weeks as a therapeutic measure.

This has been under trial as a therapeutic agent in Indian childhood cirrhosis and post-viral hepatitis cirrhosis in our clinic at Madras in recent years. There have been a few other cases of reversal of less extensive fibrosis in our series at Madras.

In our experience in Madras, where we still see a number of infants with congenital syphilis, it does not seem to be responsible for childhood cirrhosis except perhaps in rare instances. This statement is based both on the negative serological findings in our series of cases of childhood cirrhosis in Madras, and on the study of liver biopsy materials from infants with active congenital syphilis. The pericellular fibrosis associated with congenital syphilis in textbook descriptions has been found in only one of the 31 infants with active manifestations of congenital syphilis on whom liver biopsy studies were undertaken. This solitary patient was an infant, aged one month, with overwhelming syphilitic septicæmia, who died a couple of days after admission to hospital. All the others showed only a picture of subsiding hepatitis. Perhaps overwhelming prenatal syphilitic infection sometimes gives rise to pericellular mesenchymal reaction; but then such fœtuses seem to die in utero or soon after birth.

[1] For Figures I and II see art-paper supplement.

Conclusion.

In conclusion, I should like to add that further light on the understanding of the ætiological aspects of childhood cirrhosis of undetermined origin in India and elsewhere in the world is likely to be shed with the newer techniques in viral studies. Animal experimentation is also likely to throw further light on dietary fibrosis of the liver.

Reports of Cases.

AN UNUSUAL CASE OF PHENYLKETONURIA.[1]

By IAN C. LEWIS, M.D., M.R.C.P., D.C.H.,
Senior Assistant, Department of Child Health, University of Western Australia, Perth.

PHENYLKETONURIA is a heredo-familial disorder transmitted by an autosomal recessive gene, and due primarily to an absence or a deficiency of the enzyme phenylalanine hydroxylase carried by the allele of that gene in normal subjects. The disorder is characterized clinically by mental retardation and identified by the presence of phenyl pyruvic acid and other phenol substances in the urine. Physical growth is usually unaffected.

The disorder is now easily diagnosed after the first few weeks of life by simple urine tests—the ferric chloride test and now the "Phenistix" test (Ames).

The following case is remarkable for certain unusual features. In an endeavour to avoid interference with normal mental development, physical growth was interrupted to such an extent that death appeared imminent, even though on theoretical grounds enough phenylalanine for adequate growth had been provided. When treatment was abandoned, physical recovery was immediate and dramatic. With subsequent treatment, both growth and development advanced so rapidly that, not withstanding the traumatic experiences of prolonged hospitalization for a young infant, the patient now, at the age of 17 months, is a well-built, sturdy little boy behaving normally for his age.

Clinical Record.

An obstetrician got into touch with Professor W. B. Macdonald in the latter half of 1958 to say that he was attending a woman who had a child, aged five years, affected by phenylketonuria. The woman was pregnant again.

The baby, A., was born on November 18, 1958, weighing 2·95 kg., and 18 days later was referred to the Princess Margaret Hospital for Children, Perth, for investigation. Although the result of the ferric chloride test was equivocal, urinary chromatography revealed excess phenylalanine, and the infant was admitted to hospital for further investigation and treatment.

Figure I shows the child's progress. Despite a diet low in, but not devoid of, phenylalanine, the infant failed to thrive. At the age of four and a half months his condition was so poor that it seemed that he would die if the diet was persisted with. After much deliberation, it was decded to abandon treatment, and he was given a normal diet of a full-strength dried cow's milk preparation. There was an immediate and dramatic response, and during the next month he gained nearly a kilogram in

[1] Read at a meeting of the Australian Pædiatric Association, Canberra, April 22 to 25, 1960.

weight. Once again a phenylalanine-poor diet was introduced, this time gradually; it took about six weeks to return the serum phenylalanine level to a satisfactory figure. However, the child continued to thrive, and it appeared, moreover, that his development was progressing normally. This impression has been confirmed by psychometric testing. A psychologist has examined him on two occasions and placed his development within normal limits for his age.

calories than the estimated requirements. Later many fruits and vegetables, a little milk and meat, and sago or cornflour may be used in the menu.

A.'s diet was made up in the following manner. He received between 30 and 40 grammes of "Cymogran", 30 ml. of milk, and 30 grammes of "Peters" special cream (about 80% fat content). At first it was considered that the failure to thrive might be due to fat intolerance, and the cream intake was reduced, calories being made

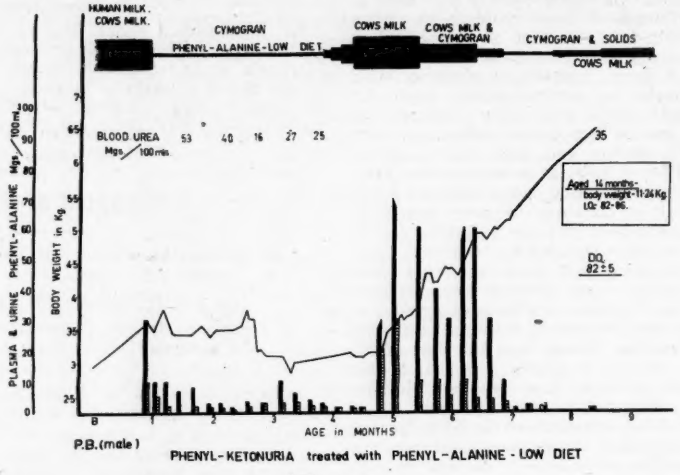

FIGURE I.

The reason why he failed to thrive in the early stages of therapy is of particular interest. It was thought that this must have been due either to (i) the presence of an additional abnormality or (ii) some dietetic factor.

The child was screened for infection, but none was found. The occasional vomiting was not sufficient to account for the poor progress. The stools were normal in appearance and in consistency. The blood urea level was within normal limits, and no serum electrolytic or urinary chromatographic abnormality was detected.

The diet seemed to be the most likely cause for the early failure to respond to therapy. In preparing a diet for babies with this condition, it is usual to give protein in the form of one of the commercially prepared phenyl-

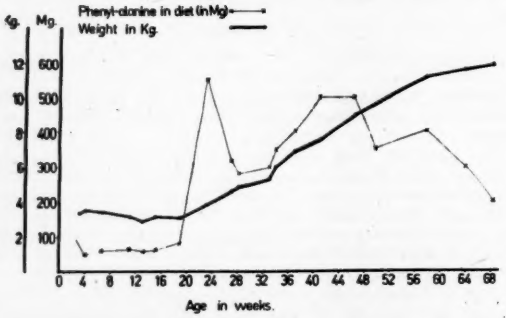

FIGURE II.

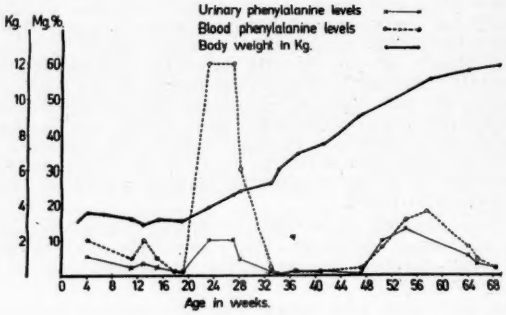

FIGURE III.

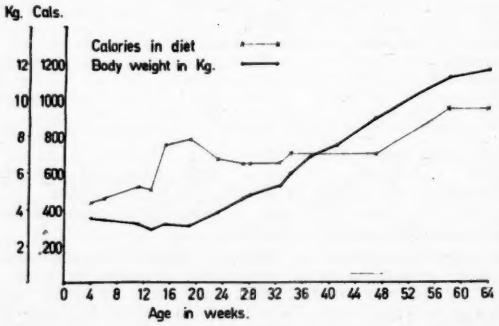

FIGURE IV.

alanine-poor preparations, such as "Cymogran", "Minafen" or "Lofenalac". Phenylalanine is an essential amino acid, and small amounts are needed even in phenylketonuria if the child is to grow. The usual allowance is 10 to 15 mg. per kilogram of body weight. Calories are added in the form of glucose and sucrose, and as cream. It is recommended that affected infants receive about 30% more

up using additional glucose. There was no improvement. The phenylalanine levels were estimated frequently and were found to be reasonably satisfactory (Figures II and III). The caloric content of the diet seemed adequate

(Figure IV). Professor Macdonald wrote to Professor A. Moncrieff describing the problem and detailing the diet given. Professor Moncrieff consulted Dr. W. W. Payne, and they suggested a list of vitamin supplements, which included some such as inositol, biotin, alpha-tocopherol and folic acid, which were not present in the multiple vitamin preparation ("Pentavite") which was being used. However, the addition of these supplements to A.'s diet made no difference to his progress.

FIGURE V.

On the other hand, there was an immediate response to full-strength milk feeds ("Lactogen"). The child's appetite improved, vomiting ceased and he gained weight rapidly. There was no relapse when he returned to his former diet.

Comment.

Why this child proved so unresponsive to the initial therapy is not known but he is at present making excellent progress.

Other people's views on this case in the light of their experiences with these very young infants suffering from phenylketonuria, and in particular an answer to the question of what made A. grow from a bag of bones to the sturdy, happy, normal little boy seen in Figure V, would be welcomed.

UNILATERAL RENAL DISEASE WITH HYPERTENSION: MEDICAL ASPECTS.[1]

By FELIX ARDEN, M.D., M.R.C.P.,
Brisbane.

BY a curious coincidence, two little girls were admitted to the Brisbane Children's Hospital in 1959 within a few weeks of one another. Both suffered so severely from hypertension that death was imminent; both were discovered to have unilateral renal disease; and both now seem to have recovered completely after nephrectomy.

My part of this joint presentation is to review the disordered physiology and present the case histories; then, as we did at the time, to make way for a surgeon, who will demonstrate the pathological findings and report the subsequent progress of the children.

One might say that our concept of the link between renal disorders and high blood pressure began with Bright, who in 1833 described cases of kidney disease with enlargement of the left ventricle. Sixty-five years later Tigestedt and Bergman found that saline extracts of the kidney contained a pressor substance which they called renin. In 1934 Goldblatt and his associates produced hypertension by partial occlusion of the renal artery; and finally Butler in 1937 recorded the first case of relief of hypertension by removal of a kidney, diseased in this instance by chronic pyelonephritis.

It is common knowledge that renal damage from a variety of causes is sometimes accompanied by hypertension and sometimes not, the variability of this relationship being most striking. However, it simplifies matters to consider unilateral disease, as we are doing, for this excludes certain possibilities—for instance, that the hypertension may be due to excretory failure. Indeed, its occurrence in a person possessing one normal and one damaged kidney, and its subsequent cure by removal of the diseased organ, forces one to believe that a pressor substance of some kind was produced on the affected side. Until recently it could have been assumed that this pressor substance was renin, the production of which leads to the formation of hypertensin in the circulation. However, as Professor Peart has now reported his inability to find any trace of renin in the renal vein blood of 26 patients in these circumstances, and as he gives other reasons also for believing that the renin-hypertensin mechanism is not involved, we must conclude that the actual pressor agent is still unknown.

The fact that a patient with unilateral renal disease may have, not only high blood pressure, but also such symptoms as polyuria, thirst and hypokalæmia, indicates that the presence of a normal kidney is not sufficient to protect its owner from the ill-effects of an abnormal one. Indeed, the influence seems to be all the other way, and it is the damaged kidney that calls the tune. For a while, sometimes for a long while, the position is reversible, and the symptoms disappear on removal of the diseased organ. But eventually—and presumably as a result of the continued hypertension—secondary arterial changes occur in the hitherto normal kidney, perpetuating the trouble and making removal of the originally damaged one valueless.

The possibility of this happening leads to uncertainty about the results of nephrectomy in cases of hypertension, even when one can be reasonably sure that there was at the beginning only unilateral disease. It may also lead to hesitancy about advising operation. Renal biopsy, although not considered in either of our cases, is a useful diagnostic tool under these conditions, particularly when both kidneys function more or less evenly, but one is suspected. There is no point in performing biopsy on an apparently healthy kidney when the diseased one has negligible function, for then there is nothing to lose, and perhaps much to be gained, by an operation.

In most cases only two questions need to be answered: Is the hypertension of renal or of extrarenal origin? And, if the former, is only one kidney affected, or both? If there is unilateral kidney disease, and if the symptoms are severe, I can think of no good reason for deferring nephrectomy. This applies particularly to children, for in their few years the condition can have been in existence for only a relatively short time, and the prospects of cure are correspondingly bright.

In general, one can say that the younger the patient, the better the outlook. In Yates-Bell's recent series, only 22 of 58 adults obtained good results from nephrectomy, but all the eight children submitted to the same operation were cured.

[1] Read at a meeting of the Australian Pædiatric Association, Canberra, April 22 to 25, 1960.

We felt that we were unusually privileged at the Brisbane Children's Hospital to see two such children so close together.

Case I.

The first, A., aged six years, was admitted to the hospital in February, 1959. She had been complaining of severe frontal headaches for about a month, which tended to appear in the mornings, be relieved with aspirin, and return in the evenings. On most days she vomited and felt too sick to attend school. Her parents noticed that she was off her food, listless and losing weight. They had not observed giddiness, unsteadiness or visual disturbances. There was a story, possibly not relevant, of transient left facial weakness at the age of two years, and of left otitis media with left facial palsy five months before the present hospital admission. At this time albuminuria had been observed, but her blood pressure was not recorded.

A. proved to be a thin, wasted, sick-looking child, who at 38 lb. was approximately 12 lb. below average weight. Her blood pressure was 230/190 mm. of mercury, and there was clinical evidence of left ventricular enlargement. The peripheral arteries were thickened. Gross bilateral papilloedema was present, and hæmorrhages, both old and recent, were visible in both optic fundi, with a few patches of exudate. Except for residual left facial paresis, no organic signs of a lesion of the central nervous system were discovered. Her urine contained albumin varying from "half" to "a cloud". Microscopic examination revealed up to 10 leucocytes and up to 6 erythrocytes per high-power field, with occasional hyaline, granular and cellular casts. She was thirsty, and passed a large quantity of dilute urine, daily specific gravity readings ranging from 1004 to 1012. The highest specific gravity achieved after restriction of water intake was 1015. The blood urea levels were between 20 and 45 mg. per 100 ml., and the urea clearance reached 88% of the average normal figure. The serum electrolytes, estimated on two occasions, were normal with regard to sodium, chloride and carbon dioxide, but very low figures were obtained for potassium (2·7 and 2·3 mEq/l. respectively). Lead poisoning was excluded by the negative history, negative X-ray findings in long bones and absence of stippled cells from the blood film. The result of the "Regitine" test was negative, and there were only normal quantities of pressor amines in the urine (26 μg. in 24 hours). The X-ray films were most interesting, revealing a calcified area near the upper pole of the right kidney, thought to be calcification in an aneurysm of the renal artery.

While being investigated, A.'s condition went from bad to worse. Her headaches became increasingly severe, especially at night. Her blood pressure fluctuated between 230 and 250 mm. of mercury, systolic, and 170 and 200 mm., diastolic. Vomiting became more frequent and her appetite so poor that tube feeding was resorted to. In spite of everything, she lost another 3 lb. during her first three weeks in hospital, and at this rate could not have lived long. It was at this stage that surgical assistance was sought.

Case II.

The second child, B., aged eight years, was admitted to hospital in May, 1959. She lived in the country, and her story was of headaches most of her life, which had increased recently. During the previous eleven weeks there had been also three nocturnal episodes of intense headache, vomiting, deviation of the eyes, loss of consciousness and muscle spasms lasting for about five minutes. For some time she had been very thirsty, drinking several jugs of water a day and passing a lot of dilute urine. After the last attack she had been admitted to hospital in the country, where it was found that she had albuminuria and extremely high blood pressure. There was no story of lead poisoning or previous renal disease and no family history of epilepsy.

B. was pale and looked ill, and at 50 lb. she also was 12 lb. below average weight. Her heart was enlarged, with a thumping left ventricular impulse and an exaggerated aortic second sound. The radial arteries were thickened, and examination of the optic fundi showed early hypertensive changes, but no hæmorrhages, exudate or papilloedema. Her blood pressure was 230/170 mm. of mercury. No abnormality could be found in the central nervous system. The urine was pale and of specific gravity 1002, and contained a cloud of albumin. Microscopically it was clear, and cultural examination showed it to be sterile. The result of the water concentration test ranged from 1002 to 1016. Her blood urea content was 27 mg. per 100 ml., and the urea clearance was 64% of average normal. Urinary lead excretion (0·01 mg. per litre) was well within normal limits. There were no coproporphyrins in the urine, no stippled cells in the blood films and no dense shadows in the long bones. The result of the "Regitine" test was negative. Her pyelogram indicated a contracted right kidney, with a normal appearance on the left side. Concentration of contrast medium was poor on both sides, perhaps because of the diuresis.

Only nine days after coming to hospital, B. had an extremely severe hypertensive attack with prolonged convulsions, during which she almost died. We concluded that urgent treatment rather than further investigation was indicated, and in view of the radiological abnormality of the right kidney and the apparent healthiness of the left, we conferred with Mr. Peter Grant about performing right nephrectomy.

UNILATERAL RENAL DISEASE WITH HYPERTENSION IN CHILDREN: SURGICAL ASPECTS.[1]

By PETER GRANT, F.R.C.S.E., F.R.A.C.S.,
Brisbane.

IN both the cases reported by Dr. Felix Arden nephrectomy was performed. In each case a transverse incision was used, so as not only to remove the kidney, but also to allow for general abdominal exploration and in particular the examination of the other kidney. The anæsthetic used was similar in each case, the agents being "Pentothal", nitrous oxide and oxygen.

In Case I, that of A., the kidney was operated on by Dr. Robert Shannon, Surgical Superviser at the Brisbane Children's Hospital, while I operated in the other case.

No difficulties of any magnitude were encountered with either operation, except that in Case II (that of B.) there was some difficulty in examining the renal pedicle because the kidney was high up under the liver, and the pedicle was of necessity ligated without any attempt to divide the vessels separately.

The blood pressure of both children had begun to fall by the end of the operation, and it has remained within normal limits ever since. The actual figures for the post-operative readings are as follows:

Case I, right-sided lesion; blood pressure (millimetres of mercury):	
Before operation	240/196
One hour later	155/125
Four hours later	125/95
Seven hours later	130/100
Thirteen hours later	125/95
Next day	130/95
Second day	100/65
Two weeks later	130/90
Thirteen months later	120/90
Case II, right-sided lesion; blood pressure (millimetres of mercury):	
Before operation	230/140
One hour later	190/140

[1] Read at a meeting of the Australian Pædiatric Association, Canberra, April 22 to 25, 1960.

Two hours later	130/80
Next day	140/80
Second day	145/80
Eleven months later	120/70

Since operation, the general condition of both children has continued to improve, and they are both now very well and completely free from hypertensive symptoms.

The pathology of both kidneys is extremely interesting and is well shown in Figures I to III.[1]

Case I.

Macroscopic Description of the Kidney.

The specimen consisted of a kidney weighing 20 grammes and measuring 6·0 by 3·5 by 2·0 cm. The antero-lateral aspect was normally curved, except for a crescent-shaped depressed area at the apex, probably due to atrophy. On the postero-medial aspect the atrophy was more marked, and extended down to the lower third of this surface. In longitudinal section the cut surface showed thinning of the cortex and medulla in the upper third of the specimen, and a normal appearance in the lower two-thirds. The pelvis and ureter appeared normal.

The blood supply to the upper pole was by a tortuous artery, 5 mm. in diameter, which first curved upward where a moderate degree of stenosis is present. It then curved downwards again, and was at that point more stenotic, the lumen measuring 1·2 mm. This vessel was posterior to the pelvis of the kidney. The renal vein was anterior to the pelvis and above a small artery which supplied the lower pole. This vessel had a pin-hole lumen and dilated to form an aneurysm 1 mm. in diameter. This was connected by a narrow segment to an aneurysm 5 mm. in diameter, which narrowed to 2 mm. to supply the renal tissue.

Microscopic Description (Dr. Brian Hillcoat).

In the lower pole there were mild changes consisting of patchy glomerular fibrosis and thickening of the arterial wall. There were a few dilated tubules containing a deeply eosinophilic material.

In the upper pole there were severe changes of glomerular fibrosis, crowding of glomeruli and round-cell infiltration. The supporting connective tissue was reduced in quantity. The arteries and arterioles appeared relatively normal.

Thrombosed Larger Artery.—The wall of the artery was thickened and fibrous, and the differentiation into intima, media and adventitia was lost. There was concentric deposition of calcium in the wall. Elastic stain showed a complete absence of elastic tissue. At the first stenotic area, the longitudinal section showed a wedge of tissue invaginating the arterial lumen; it arose from one side of the vessel and was accompanied by protrusion of the media also. The media was cellular, but had lost its elastic tissue and was covered by thick fibrous tissue in which calcification had occurred. In the other wall thickening and fibrosis of the intima were present. The stenosis had narrowed the lumen to one-third, and the area contained post-mortem thrombus. At the second stenotic area, the longitudinal section showed an invagination of media covered by fibrous intima from both sides of the vessel. Patchy calcification was present, and the lumen was narrowed to one-sixth that of the vessel. The orifice contained thrombus that was organizing and almost replaced by vascular connective tissue.

Patent Smaller Artery.—The section at the first aneurysm was somewhat oblique, but marked thickening and fibrosis of the intima were evident. The media was about half the thickness of the wall, where it could be identified. Here thickening of the internal elastic lamina was also apparent. The section at the second aneurysm showed gross intimal thickening and fibrosis. The media was represented by cellular tissue comprising approximately one eighth of the thickness of the wall, and separated from the thickened intima by fragmentated and degenerating elastic tissue. In the intima were two areas of lipid-containing cells.

[1] For Figures I, II and III see art-paper supplement.

Summary.

Ante-mortem thrombosis of the severe second area of stenosis of the artery to the upper pole produced ischæmic atrophy of this pole. The lower pole received blood through the still patent artery to the lower pole, and the arterioles here showed mild changes of hypertension.

Case II.

Macroscopic Description of the Kidney.

The kidney from the child B. measured 8·0 by 5·0 by 3·0 cm., and externally the lower two-thirds showed shrinking of the renal tissue and tapered to a thin lower pole. Close to the pelvis, nodular areas projected above the atrophic tissue. The depressed areas were spotted with purpuric hæmorrhages. In longitudinal section, the cortex and medulla of the atrophic lower two-thirds were much thinned, so that the calyces were unusually prominent. The superior calyx appeared dilated as well. The cortex and medulla of the upper pole appeared normal. The pelvis and ureter appeared normal.

Microscopic Description.

Sections from the lower pole showed crowding and sclerosis of glomeruli, with a marked reduction in the number of tubules present. Those remaining had a thyroid-like appearance—they were dilated and contained deeply eosinophilic material. There were several areas of round-cell infiltration present. The larger vessels were normal. The arterioles showed thickening of their walls, but little or no proliferation of their intima.

In the upper pole, the glomeruli were normal except for some dilatation of their capsular spaces. There were occasional tubules that were dilated and contained eosinophilic material. There was spotty calcification in the medulla. The muscular coats of the arterioles were thickened, and there was intimal proliferation.

Summary.

The pathological conclusion was that a chronic disease process was present involving the lower two-third of the kidney, yet sparing the upper pole to a large extent. It was thought unlikely that glomerulo-nephritis or pyelonephritis would cause this distribution, so ischæmia of the lower pole associated with an abnormal vascular supply was the most likely ætiological basis. The arterial changes in the lower pole were consistent with proximal occlusion, those in the upper pole with hypertension.

Comment.

Because of their precarious condition we were not able to take arteriograms on either of these children. It is a pity that they were not done. There is no doubt that any child with hypertension must have the most exhaustive renal investigation. As Trippel from Northwestern University, Chicago, has pointed out, even minor lesions as shown in the intravenous pyelogram may hold the key to the problem. Many of these can be elucidated by arteriography. Already attempts are being made to repair some of these arterial defects with either arterial grafts or spleno-renal shunts.

GIANT HÆMANGIOMA WITH THROMBOCYTOPENIA.[1]

By T. Y. NELSON, F.R.A.C.S.,
Royal Alexandra Hospital for Children, Sydney.

RHODES (1944), in describing a case of giant hæmangioma with thrombocytopenia, stated that he could find a record of only one other case in the literature. Since then there have been a number of reports drawing attention to this unusual combination, but the condition is still rare in the experience of any one individual.

[1] Read at a meeting of the Australian Pædiatric Association, Canberra, April 22 to 25, 1960.

The essential features are that a baby, usually aged under 12 months, is noted to have a large subcutaneous hæmangioma on one of the limbs, in the scapular or supraclavicular region or in the axilla. This remains unchanged for several months, when there is a rapid increase in size to "giant" proportions. This change is accompanied by thrombocytopenia, although there may be very few purpuric manifestations on other parts of the body. There is anæmia due to loss of circulating blood into the tumour, and frequent blood transfusions may be necessary. Why some infants with hæmangiomas should develop this abnormality in the blood while others are spared has not been satisfactorily explained. Some of the theories that have been advanced are as follows:

1. That the thrombocytopenia is dependent on excessive destruction of platelets in the tumour (Good, 1955). It is suggested that in this condition sequestration of platelets occurs in the tumour, whereas in essential thrombocytopenia it occurs in the spleen.

2. That platelet destruction occurs through the formation of antibodies (Weissman, 1953).

3. That rapid removal of platelets occurs in the dilated capillaries of the hæmangioma. The tumour may have some special characteristics that attract and hold platelets (Diamond, 1956).

Whatever the cause of this condition, some idea of the clinical features can be gathered from the various cases reported. (i) The condition occurs only with large hæmangiomas. (ii) Improvement in the blood picture occurs only when the tumour regresses (either spontaneously or with benefit of X-ray therapy) or is removed surgically. (iii) No benefit follows removal of the spleen. (iv) The abnormal blood condition may persist for long periods (even many months). (v) Deaths have occurred in untreated cases, and in some in which X-ray therapy has been given.

Since 1953 this condition has presented on three occasions at the Royal Alexandra Hospital for Children, and each case showed some different features.

Case I.

A girl, aged nine months, was admitted to the Institute of Child Health on May 22, 1953, under the care of Professor Lorimer Dods, with an ulcerated tongue and a swelling under the mandible. Rapid enlargement of the tumour had occurred prior to her admission, with evidence of an accumulation of blood under the skin, and a number of petechiæ were evident over the body. The spleen was not enlarged, and laboratory tests showed that the bleeding time was 12 minutes, the coagulation time 14 minutes, the hæmoglobin value 11·4 grammes per 100 ml. the number of platelets 53,000 per cubic millimetre. After a transfusion the hæmoglobin value was 13·8 grammes per 100 ml., but the platelets still numbered only 40,000 per cubic millimetre. In the history it was noted that the child had always had the appearance of a "double chin", suggesting that an angioma had been present since birth.

On May 25, the tongue was pushed up to the roof of the mouth, and there was a tense submandibular swelling. Profuse nasal secretion was present and continued until May 31, when tracheotomy was performed owing to a rapid increase in respiratory obstruction. The child had received cortisone up to this time without improvement, and as an emergency measure splenectomy was performed under local anæsthesia and with "Pentothal" given per rectum. No improvement followed this operation, and the child died on June 11. Examination of the tumour at autopsy showed that it was a hæmorrhagic growth with marked invasive properties, neoplastic tissue extending directly into the muscles of the floor of the mouth and tongue. There was also a small neoplastic growth (possibly metastatic) beneath the periosteum of the neck of the right femur. Examination of the bone marrow showed hyperplasia, and megakaryocytes were present in excess, so that thrombocytopenia could not be accounted for by reduction of megakaryocytes.

Case II.

A girl, aged four months, was admitted to hospital on July 9, 1956, under the care of Dr. J. Steigrad. She had been born with a large hæmangioma on the right thigh. The limb had increased in size, until at the time of her admission to hospital it was estimated to be three times as large as the normal limb. The appearance was that of a hard brawny swelling with some petechiæ around it. She had had treatment with cortisone before her admission. The first blood examination showed a hæmoglobin value of 8·5 grammes per 100 ml. and numerous platelets were noted. It was only in subsequent blood examinations that reduction in the number of platelets was seen. On July 13, a biopsy specimen was taken, and Dr. R. D. K. Reye reported that throughout the dermis and extending into the subdermal fat and fibrous septa there were many discrete and connected lobules of endothelial proliferation. A large proportion of these endothelial cells were canalized to form capillary vessels, but the degree varied from lobule to lobule. His comment was:

> The tumour appears to be growing rather actively at the present time and it is interesting to note that in the lumen of some of the capillary vessels there are large cells of megakaryocytic type. The only tumour of this type I have seen containing similar cells was associated with severe thrombocytopenia.

A marrow biopsy showed no numerical increase of megakaryocytes, the number studied being 58 cells. No platelets were seen in any specimen. The morphological characteristics of the megakaryocytes were similar to those seen in idiopathic purpura.

On July 23, a course of deep X-ray therapy was started; the total dosage given was 2000*r*. By August 1, considerable improvement had occurred, and the child was discharged from hospital to out-patient supervision.

Case III.

The most recent case occurred in December, 1958. The patient was a boy, aged three weeks, whom I examined on that date. This baby had a large subcutaneous hæmangioma of the left thigh. Small nodules were felt through its substance, which suggested that thrombosis was occurring and might result in natural regression. No treatment was suggested at that stage.

In February, 1959, the child was examined again, with the history that for some time the tumour had been enlarging, but that in the last week there had been a sudden increase in size. The thigh was very swollen, with evidence of a large subcutaneous collection of blood. The hæmoglobin value was 8 grammes per 100 ml. After the baby's admission to hospital a transfusion was started and a small incision made over the swelling. This liberated 8 oz. of blood-stained fluid, with almost complete disappearance of the swelling. In a few days the swelling recurred, and petechial spots appeared on the abdominal wall. Blood examination at this stage showed that the hæmoglobin value was 11 grammes per 100 ml. and that the thrombocytes numbered 15,000 per cubic millimetre. On marrow biopsy, the megakaryocytes showed decreased platelet formation and resembled those seen in idiopathic thrombocytopenic purpura.

Arrangements were made for the child to have deep X-ray therapy to the tumour and this was commenced on February 18. The course amounted to 1500*r*. For the next four months there was little change in the child's condition. No diminution in size of the tumour occurred as a result of the X-ray therapy, and frequent transfusions were necessary. The number of platelets remained persistently low, but no further purpuric manifestations were seen. By the fifth month a further increase in size had occurred, and an exuberant growth of angiomatous tissue had ulcerated the skin anteriorly, leaving a raw surface. This was infected and foul-smelling, and attempts to clear up the surface infection met with little success. A further course of deep X-ray therapy started on August 10 had no effect, and it appeared that removal of the limb was the only hope of arresting the condition. Up to this time 16 transfusions had been necessary.

ILLUSTRATIONS TO THE ARTICLE BY S. T. ACHAR.

FIGURE I.

Photomicrograph of the liver (surgical biopsy specimen) from a girl, aged nine years, with cirrhosis of the liver and evidences of portal hypertension. Previous history suggestive of viral hepatitis three years earlier. Picture shows well-marked fibrosis with macroscopic and microscopic nodules. (Gömöri's reticulum stain, × 80.)

FIGURE II.

Photomicrograph of the liver (needle biopsy specimen) from the same child as in Figure I, two years later. Picture shows normal architecture and no fibrosis. (Gömöri's reticulum stain, × 80.)

ILLUSTRATION TO THE ARTICLE BY PETER GRANT.

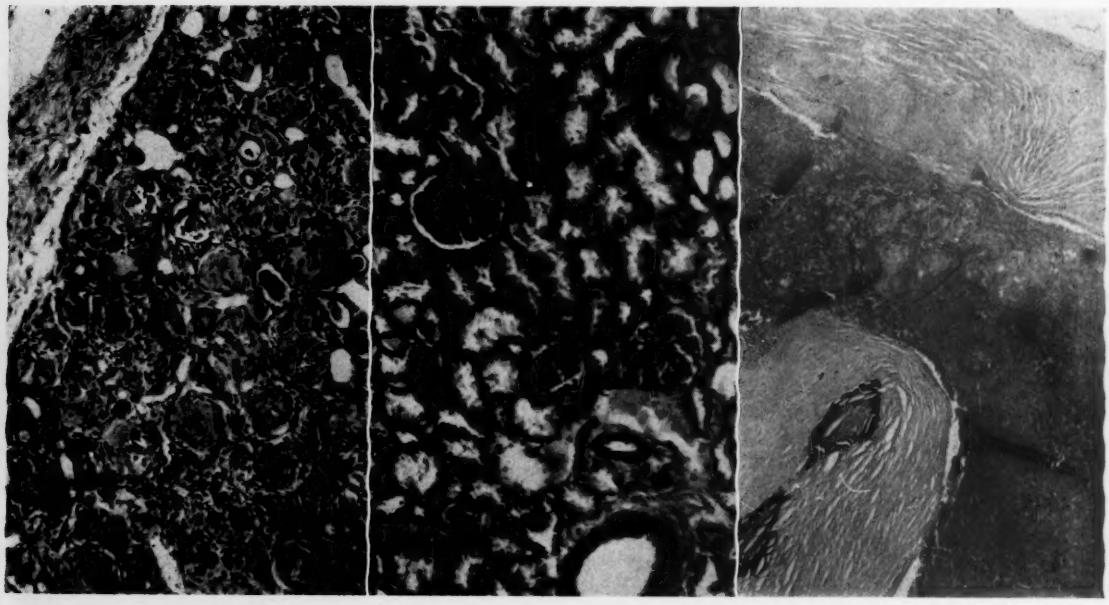

FIGURE I.

Section showing effect of ischæmia in upper pole of kidney — pole with thrombosed artery.

FIGURE II.

Lower pole, same kidney; no ischæmic effect, but hypertensive changes in vessels.

FIGURE III.

Thrombosis and calcification in wall of artery to upper pole of kidney.

On September 25, amputation through the left hip joint was performed. There was sufficient tissue posteriorly to provide a flap, although it was grossly œdematous and discoloured, and it was difficult to know how much angiomatous tissue was present in this area. Preliminary ligation of the internal iliac vessels was carried out extraperitoneally on the left side through a low oblique abdominal incision, and through a similar incision on the right side a clamp was placed temporarily on the right common iliac artery. The limb was rapidly removed, without gross hæmorrhage, but with a good deal of capillary oozing. After removal of the clamp on the right side hæmorrhage was easily controlled, and after the limb was removed no abnormal oozing occurred. Six hundred millilitres of blood were transfused during the procedure. Healing was satisfactory, and the thrombocytopenia stopped immediately.

Since operation the baby has progressed satisfactorily and the blood count has returned to normal. Examination of the specimen showed that the abnormality was confined to the superficial tissues. There was a uniform increase in bulk in the soft tissues 6 cm. thick. The muscles were pale, reduced in bulk and œdematous. Microscopic examination showed the tumour tissue to contain a large amount of blood, some in thin-walled capillary vessels, but much more in a loose mesh between the vessels, and in these lakes a few islands of hæmatopoietic tissue were seen. Dr. Reye commented:

> Though in essence a capillary hæmangioma, this tumour obviously has unusual growth potential which would cause local progression. There is no histological evidence to warrant classifying it as an angiosarcoma.

Discussion.

The first case was an example of a malignant tumour (hæmangioendothelioma) infiltrating the tongue, with a possible metastasis in the femur. It is of interest that thrombocytopenia can occur in association with this malignant type of metastasizing tumour as well as with the more benign type of malformation exemplified in the other two cases. It appears that this particular association of thrombocytopenia with malignant hæmangioma is confined to the early years of life, as there is no mention of it in the reported cases of hæmangioblastomas in adults commonly originating in the breast (Tibbs, 1953; Patrick *et alii*, 1957).

The second case followed the more usual course of recovery after X-ray therapy, but in the third case, X-ray therapy had no effect.

The most important point for discussion is the question of the place of X rays in treatment. In all the earlier reports they are regarded as the sheet anchor on which to rely for regression of the tumour. Cortisone has been used in some cases with very doubtful benefit.

Rhodes (1944) stated that there was no precedent to follow with regard to X-ray dosage, and when the early doses were ineffective he increased the amount given and finally obtained regression. In another case (Silver, 1948), X-ray treatment seemed to be successful at first, but the tumour later increased in size and further X-ray treatment had no effect. This child finally died. It was suggested that the more adult type of hæmangioma (cavernous), being composed of large sinusoids, was less sensitive to radiation than the capillary type.

Predominance of cavernous tissue may account for lack of response to X rays. To support this contention, a tumour that responded rapidly to X rays (Southard, 1951) was shown by biospy to consist predominantly of capillary tissue.

In two other cases (Weissman, 1953), the amount of X rays given was only 300r, and the author considered that it was doubtful whether this had any effect on the tumour, and that natural regression probably occurred.

So far in the literature little mention has been made of the place of radical surgery in this condition. In one report (Good, 1955), surgical excision in two stages was carried out at a later stage after X-ray therapy had been ineffective, but the more usual procedure has been to wait patiently for regression of the tumour.

In one case (Weissman, 1953), the number of platelets remained under 18,000 per cubic millimetre for six months, and it was not until 15 months after the patient's first admission to hospital that the platelet count returned to normal and reduction was noted in the size of the tumour.

The unfortunate ending to Case III in this report, in which amputation of the limb was finally necessary, raises the question whether radical surgery should be undertaken more frequently in the early stages of this condition.

In a recent case report (Johnson, 1959), the author took this view, and when faced with a tumour which must have been very similar to that in the present Case III, but which involved the whole lower limb, decided on early excision in two stages in the manner of the Kondoleon procedure. At the first stage a long incision on the outer side of the limb was made, and abnormal tissue was removed down to the deep fascia. The skin was replaced, and two weeks later the remaining tumour tissue was removed through an incision on the inner side of the limb. The result was very successful.

The inescapable conclusion to be drawn from a consideration of all these facts is that, if one is faced with the problem of a baby with a large cavernous hæmangioma, the wise course to follow is to excise it early before thrombocytopenia has developed. This is usually not a major procedure, and in many cases the skin can be preserved. If excision of some skin is necessary, it can be replaced by a skin graft (Paletta, 1959).

At the moment there is a wave of enthusiasm for conservative treatment of hæmangiomas, and large series have been produced to show that over 50% of these abnormalities will regress if left alone. There can be no criticism of this approach if it is confined to small subcutaneous hæmangiomas and strawberry marks; but the implications of large hæmangiomas are quite different, and early excision is advisable.

Summary.

Three cases of the syndrome "giant hæmangioma with thrombocytopenia" are reported. The first occurred in an infant with a malignant hæmangioendothelioma invading the muscles of the tongue and neck, and was fatal. In the second the tumour responded to X-ray therapy, and the patient was sufficiently recovered in one month to be discharged from hospital. The third patient failed to improve after X-ray therapy, and was finally cured by amputation of the limb.

The question of X-ray therapy is discussed, and a plea is made for early excision of large cavernous angiomas before thrombocytopenia has developed.

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Reviews.

The Physical Health of Children. By Audrey Kelly; 1960. Mitcham, Victoria: Penguin Books, Pty. Ltd. 7¼" × 4¼", pp. 256. Price: 5s. 6d.

THIS book has been published in the "Penguin" series, and has been written to supply mothers with an elementary knowledge of child care, and of some of the common and abnormal conditions that can occur. Presumably it is intended to compete with Benjamin Spock's "Baby and Child Care", for the English public at least. However, it must inevitably fail to do so, as it has neither the authority nor the charm of its competitor. The subject matter is limited to physical care, and is reasonably accurate and comprehensive, though there are a few strange statements —such as that "brain damage can be caused in hæmolytic disease by deposition of destroyed blood cells in the brain", and that "sticky eyes in the newborn can be cured with penicillin eye drops", also that "paronychia can be prevented by keeping the nails cut". There are sections on feeding and general management, infectious diseases and common illnesses. The subjects in general are dealt with simply but seriously, so the book does not make easy reading for mothers. We consider the whole approach too dogmatic, and believe that greater authority than being "a doctor who is also a mother" was required to write a book like this. Being a mother teaches a great deal about children, as does doing welfare work; but no authorities are quoted for opinions, and we cannot but think that if a book for mothers is to be recommended, it should be by Illingworth or Spock.

Notes on Infant Feeding. By Stanley Graham, LL.D., M.D., F.R.C.P. (Ed.), F.R.F.P.S. (Glas.), and Robert A. Shanks, M.D., M.R.C.P. (Lond.), F.R.F.P.S. (Glas.); fifth edition; 1960. Edinburgh and London: E. & S. Livingstone Ltd. 7¼" × 4¾", pp. 76. Price: 4s. 6d. net (English).

THIS excellent little book has been written to meet the needs of medical students. However, it will be found very useful by nurses and doctors supervising mothers and babies. It is simple, accurate and comprehensive; it covers the subject of breast feeding and its common problems, and deals with such special conditions as the care of premature infants, failure to thrive and vomiting and diarrhœa. The text is scientific but conservative, and guided by common sense. It includes details of feeding techniques such as gavage, as well as details of the feeds. There is an appendix that contains useful information on normal development of children, such as ossification centres, head circumference, dentition, etc. This book can be highly recommended.

Antithrombotic Therapy. By Paul W. Boyles, M.D.; 1959. Modern Medical Monographs, No. 20. Irving S. Wright, M.D., Editor-in-Chief; Richard H. Orr, M.D., Consulting Editor. New York, London: Grune & Stratton, Incorporated. 8½" × 5½", pp. 142, with many illustrations. Price: $5.00.

THIS monograph sets out to discuss the many aspects, both clinical and laboratory, of the treatment of thromboembolic disorders. The main text (79 pages) is divided into seven chapters. The first two cover the theoretical and practical aspects of blood coagulation. The third chapter briefly describes the naturally and pathologically occurring antagonists of coagulation and the therapeutic devices which have been used clinically. The next three chapters are devoted to the practical considerations and the hazards of anticoagulant therapy and the difficulties in evaluating the effects of treatment. The concluding chapter details the present knowledge of various clot-lysing substances.

There is a large bibliography (15 pages), and an addendum (29 pages) describes the technical aspects of tests performed in the coagulation laboratory. This general arrangement appears satisfactory.

Unfortunately this book does not fill the need which exists for it, as its defects are numerous. Owing to a lack of balance in it, the experienced physician will find little that is new or thought-provoking, whilst brevity has resulted in inadequate detail for the novice. Few of the aspects it covers are dealt with completely. There is practically no discussion on the anticoagulant drugs themselves or on the problems of control of their dosage. The large addendum, owing to unevenness in detail, does not provide a suitable reference for the coagulation laboratory. It is difficult to understand why the platelet-counting technique is described in detail when the whole-blood clotting time test, a much more difficult test, is described in a few lines.

Conflicting statements, some of which cannot be untangled, and serious errors further mar this work. As examples, it is stated that deficiency of Stuart-Prower factor is, and is not, detected by the one-stage prothrombin time test, and the table of synonyms for the clotting factors is not in accord with the source quoted. The choice of some treatment charts and the reproduction of many photographs is poor.

Owing to an apparent lack of care, omissions and assumptions of facts which are contentious, the reader of this book seeking in it a comprehensive work on the problems associated with antithrombotic therapy will be disappointed. We wonder whether the author's confusion will not add to rather than remove that of the ordinary reader.

Pædiatric Tutorials: The Newly Born Infant. By Andrew Bogdan; 1959. Sydney: Angus & Robertson, Limited. 7⅞" × 3¾", pp. 38. Price: 4s. 6d.

THIS little book appears to be in the nature of an experiment to replace roneoed notes for medical students. It consists of notes on the care of the newborn, with a blank page opposite each page of notes for the student to insert his own notes. It includes descriptions of the common conditions occurring in the neonatal period, but as its stands is not comprehensive enough for the notes of medical students. Most tutors in diseases of the newborn will probably prefer to write their own notes, but if not, this booklet could be useful with some alterations and considerable additions. For example, "Care of the Premature Infant" is quite inadequate to enable any doctor to supervise such a baby, and "Care of the Hæmolytic Disease of the Newborn" gives insufficient guidance even for emergency treatment. Most of the information is accurate; but it is irritating to find hæmoglobin values quoted in percentages, and there are some doubtful definitions—for example, maturity as the "physical, emotional, intellectual and sexual". Altogether the book will not find much sale to students where neonatal pædiatrics are being taught well; but the idea of such a book is a good one.

Physiology in Industry: Evaluation of Industrial Stresses by the Physiological Reactions of the Worker. By Lucien Brouha, M.D., D.Sc., with a chapter by John A. Zapp, Jr., Ph.D.; 1960. Oxford, London, New York, Paris: Pergamon Press. 9" × 6", pp. 158, with tables. Price: 40s. (English).

THE physiology presented in this book is not fundamental; it is sometimes superficial and frequently empirical. The experiments described sometimes give the impression that they are inadequately controlled—insufficient stress is given to the inevitable alteration in environment produced by any observations made on men in the course of their work—and some of the generalizations seem to be based on inadequate data or at least on data requiring more elaborate presentation and more critical analysis. Appropriate statistical treatment is rarely mentioned. However, having regard to the wide scope of the work, to its aims and readers, and to the fact that it largely reflects the varied experience of a single group, these criticisms are of minor importance. The authors have produced a simply-written and easily-read book, which gives not so much the answers as the methods by which the answers may be obtained to problems arising in everyday industrial activities; the methods are illustrated by numerous pertinent examples drawn from an extremely wide range of human activities. The opening chapters deal with physiological aspects of muscular activity, particularly in relation to environmental "climate"; the evaluation of heat stress is further considered in a later section, which also discusses physical and chemical environmental factors. Later chapters relate to the physiological assessment of the job itself in terms of cardio-vascular and respiratory response, and physical and physiological work. Various methods of reducing stress and fatigue in all these circumstances are described, and some indication is given of the relatively simple techniques used in deciding on the means to be adopted and their ultimate efficacy. Finally, there is

a chapter on the selection, placement and supervision of workers.

The use of symptoms as an index of the presence or absence of an industrial hazard is a well-recognized principle. The chief message of this book is that physiological reactions to work and environment may serve as indices of efficiency or fatigue. The authors stress the simpler methods of physiological assessment (such as pulse rate) appropriate to surveys under working conditions, and they indicate how such surveys may be done, how conditions may be tested, how they may be adjusted, and how they may then be retested. Time, motion, effort and environment are the essential parameters: speed, position, movement and environmental control are among the factors which may be varied appropriately after analysis of the worker, the job and the environment in terms of physiological reactions. This book is strongly recommended to all concerned with industrial medical practice, even if some of the conclusions are to be treated with reserve.

Viral Infections of Infancy and Childhood: A Symposium of the Section on Microbiology, The New York Academy of Medicine. Edited by Harry M. Rose, M.D.; 1960. New York: Paul B. Hoeber, Inc. Medical Division of Harper & Brothers. 9" x 5¾", pp. 256 with illustrations. Price: $8.00.

THIS publication is a collection of 16 papers presented by leading authorities and research workers on virus diseases. Data are presented simply enough to be easily followed by the pædiatrician unfamiliar with the newer virus techniques. Virologists would find the book of limited value, as most of the papers review work already published. By far the greatest bulk of the text is concerned with enteroviruses and respiratory tract viruses. Alexander and Colter discuss the infectivity of virus ribonucleic acid. Interesting clinical and epidemiological aspects of Coxsackie and ECHO virus infection are discussed by Dalldorf, Sabin, Melnick, Huebner, Bell, Rosen, Tyrrell, *et alii*. Influenza vaccination is considered by Davenport, Hennessy and Curnen, and the properties and production of "interferon" by inactivated influenza virus are outlined by Isaacs. Chanock and his co-workers and Rowe give an account of some of the newer respiratory tract viruses with emphasis on the hæmadsorption agents, respiratory syncytial virus and adenoviruses.

Antibiotics and Sulphonamides in Ophthalmology. By Arnold Sorsby and Joseph Ungar; 1960. London, New York, Toronto and Melbourne: Oxford University Press. 6¾" x 4", pp. 128. Price: 20s. 9d.

THIS small book in the Oxford antibiotic series contains a wealth of information on the scientific use of these drugs. If the principles laid down in this book were observed, many of the problems associated with the use of antibiotics and sulphonamides—for instance, drug resistance—would never arise.

The volume is divided into three parts. In the first part basic considerations are dealt with, pharmacology and therapeutics of individual drugs form the second part, and the third part deals with specific diseases and their treatment.

The authors do not recommend the topical use of sulphonamides in acute infections, although many clinicians have had success with their use. They point out the fact that the parenteral use of chloramphenicol produces such poor concentration in the intraocular fluids as to be useless in the treatment of intraocular infection. Great stress is laid on subconjunctival injections of penicillin, streptomycin, framycetin, polymyxin and neomycin in intraocular infections. The prophylactic use of penicillin in minor infections and injuries is deplored — neomycin, polymyxin and bacitracin are much preferred. All ophthalmologists will find this volume most helpful. It should prove a useful guide to the treatment of ocular infection.

Synopsis of Gynecology. By Robert James Crossen, M.D., Daniel Winston Beacham, M.D., and Woodard Davis Beecham, M.D.; fifth edition; 1959. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Limited. 7¾" x 4¾", pp. 340, with illustrations. Price: £3 11s. 6d.

IN this, the fifth edition, the original author, R. J. Crossen, has the assistance of D. W. Beacham and W. D. Beecham, of New Orleans. The book is attractive in appearance, the paper and printing are good. It is not written in summary style, and in this regard is an improvement on many medical synopses. It is for students only, and even then can be only an addition to ordinary textbooks. There are occasional misspelt words and misplaced or omitted letters.

In our opinion the book is unbalanced. Some conditions are given a lengthy description, others very scant mention or none at all. Metropathia hæmorrhagica is not mentioned. Almost half the book (148 out of a total of 332 pages) is given over to anatomy, physiology, diagnostic tests and methods of investigation. Consequently the presentation of the various diseases and disorders is somewhat condensed, some more than others.

The ideas and methods of treatment are modern in concept, though we do not agree with all statements; for example, we do not believe that the majority of sufferers from stress incontinence of urine will be cured by perineal muscle exercises, or that a smear test is the first procedure in post-menopausal bleeding, or that sarcoma botryoidis is invariably fatal.

The section on endometriosis is well done, and then follow some excellent pages on psychosomatic aspects of gynæcology. The discussion on treatment of carcinoma of the cervix is well presented.

Surgical techniques are very briefly described, which is probably a good thing in a students' synopsis. The chapter on ovarian tumours could be improved.

It must be remembered that this is a synopsis, and as such the text must be curtailed; but we think that the curtailment is irregular.

The Dynamics of Psychiatric Drug Therapy. Edited by G. J. Sarwer-Foner, M.D., with a foreword by D. E. Cameron, M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd. 9" x 6", pp. 654. Price: £6 8s. (English).

THE material contained in this volume consists of a series of papers read at a conference held under the ægis of the Departments of Psychiatry of McGill University and Queen Mary Veterans Hospital, Montreal. Each paper is followed by a discussion, apparently recorded verbatim.

The publication of the proceedings of various conferences in a form such as this is becoming increasingly common. After reading the contents of this volume, one is seriously tempted to wonder why. For the most part the material consists of an attempt at an uneasy synthesis between pharmacology and psychoanalysis, and contains some of the finest examples of woolly theorizing that it has ever been our privilege to read. This reaches a climax in a paper by Ostow entitled "The Effects of the Newer Neuroleptic and Stimulating Drugs on Psychic Function". It is to the credit of some of the participants that in the subsequent discussion Dr. Ostow is quite severely taken to task. As one discussant remarks (page 201):

> There seems to be a confusion of identities. Pharmacologists, overwhelmed by the complexities of studying behavioural effects, have turned into experimental psychopathologists. Psychiatrists impressed by so many new data or [sic] neurochemistry and brain function have assumed the role of clinical pharmacologists. And now I see that psychoanalysts make astounding efforts to synthesize neuro-anatomy and ego psychology. Astounding is almost too mild an adjective.

Perhaps Dr. Clifford Scott, chairman of one of the sessions, made an apt comment when he stated:

> The doctors who prescribe and the pharmacists who dispense are not many centuries removed from the alchemists who wished to change dross into gold.

He himself then joins their ranks with some comments on the significance of "the breast-like pill and the penis-like capsule". Oh dear!

No more, perhaps, need be said, other than to point out that a fairly consistent shower of misprints indicates that more attention might have been given to editing, and that, considered overall, the price of dross seems excessive.

Arthritis and Allied Conditions: A Textbook of Rheumatology. Edited by Joseph Lee Hollander, M.D.; sixth edition, 1960. Philadelphia: Lea & Febiger. Sydney: Angus & Robertson Ltd. 9¼" x 5¾", pp. 1306, with 417 illustrations. Price: £11.

THIS textbook of rheumatic diseases was first published in 1940 by Dr. Comroe, and now this is the sixth edition, edited by Dr. Joseph Hollander, Chief of the Arthritis Clinic of the University of Pennsylvania at Philadelphia. The book has been completely revised. Several sections are written by prominent authorities in the field of rheumatic disease, and include recent developments which have been gleaned from reports of medical meetings, conversations

and correspondence with other workers, as well as original work, some of which has not been published elsewhere.

Nineteen new chapters have been added. These include: "The Study of Connective Tissue", "The Rheumatoid Factor", "The L.E. Phenomenon", "Evaluation of Rheumatoid Arthritis" and "Special Drugs used in Rheumatoid Arthritis". A special section on stress in relation to rheumatoid arthritis is written by Dr. Hans Selye. Sixteen other chapters have been entirely reorganized and rewritten, and the whole volume is for all practical purposes a new book.

The sections are well written, carefully edited and well illustrated. Also there is an ingenious collection of box summaries for readers who wish to revise their reading. An extensive bibliography is given at the end of each section for those who wish to extend their studies.

It is the most comprehensive book of its type in this field of medicine, and is written not only for the specialist physician, but for research workers, orthopædists and post-graduate students of medicine. It has gained great popularity in America, and this new edition will increase its popularity elsewhere.

It is difficult to find any criticism of the book, as the standard is so high. It is noted that the American rheumatologists still regard ankylosing spondylitis as rheumatoid arthritis; but this is not agreed with by Continental and British writers, who regard it as a separate disease entirely.

Dr. Cecil, editor of a textbook of medicine which has been universally used, in writing the preface to this volume, describes it as "The Bible of Rheumatology", and this does not appear to be an exaggeration. It stands supreme as a textbook in this field. Dr. Hollander and his group of collaborators have given us a book which will be read with gratitude by all physicians interested in rheumatic disease. It should be obtained for all worthwhile medical libraries as a standard reference book.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Social Rehabilitation of the Subnormal", by Herbert C. Gunzburg, M.A., Ph.D. (Vienna), F.B.Ps.S.; 1960. London: Baillière, Tindall and Cox. 8½" × 5½", pp. 282, with illustrations. Price: 27s. 6d. (English).

"Surgery in the Aged", edited by Frank Glenn, M.D., S. W. Moore, M.D., and John M. Beal, M.D.; 1960. New York, Toronto and London; McGraw-Hill Book Company, Inc. 10" × 7", pp. 548, with illustrations. Price: $17.50.

"Cerebral Palsy and Related Disorders: A Developmental Approach to Dysfunction", by Eric Denhoff, M.D., and Isabel Pick Robinhault, Ph.D.; 1960. New York, Toronto and London: McGraw-Hill Book Company, Inc. 9" × 6", pp. 432. Price: $12.00.

"Electron Microscopy of the Cardiovascular System: An Electron Microscopic Study with Applications to Physiology", by Bruno Kisch, M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications. 9" × 5¾", pp. 192, with illustrations. Price: 60s. (English).

"Glossary of Words and Phrases Used in Radiology and Nuclear Medicine: Prepared from Various Sources for Medical Students and Residents in Radiology", by Lewis E. Etter, B.S., M.D., F.A.C.R.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications. 9½" × 6¼", pp. 220. Price: 68s. (English).

"A Review of the Mosquito Fauna of the South Pacific (Diptera: Culicidæ)", by M. O. T. Iyengar; Technical Paper No. 130, July, 1960. Noumea, New Caledonia: South Pacific Commission. 10" × 8", pp. 106. Price: 6s. (English).

"Microbes, Men and Monarchs: A Doctor's Life in Many Lands", The Autobiography of Aldo Castellani; 1960. London: Victor Gollancz Ltd. 8½" × 5¼", pp. 290, with illustrations. Price: 25s. (English).

"A Petrologic Investigation of the Manlius and Coeymans Limestones", by Franklin W. Fessenden; *Annals of the New York Academy of Sciences*, Volume 84, Art. 8; June 24, 1960. New York: The New York Academy of Sciences. 9" × 6", pp. 285-302. Price: Not stated.

"Diffusion Behavior of Supersaturated Binary Solutions", by Jacob Mazur and Tumer Alfrey, Jr.; *Annals of the New York Academy of Sciences*, Volume 84, Art. 7, June 24, 1960. 9" × 6", pp. 251-284. Price: Not stated.

"A Short History of Obstetrics and Gynecology", by Theodore Cianfrani, M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd. 9" × 5¾", pp. 468, with illustrations. Price: £5 (English).

"An Introduction to Physical Anthropology", by M. F. Ashley Montagu; third edition; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications. 9" × 5¾", pp. 788, with illustrations. Price: £5 16s. (English).

"A History of Psychiatry", by Jerome M. Schneck, A.B., M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd. 9" × 5¾", pp. 208. Price: 44s. (English).

"Electroencephalography in Anesthesiology", by Albert Faulconer, Jr., M.D., M.S., and Reginald G. Bickford, M.B., Ch.B., M.R.C.P.; 1960. Springfield, Illinois: Charles C. Thomas, Oxford: Blackwell Scientific Publications. 9" × 5¾", pp. 98, with illustrations. Price: 38s. (English).

"Neurology Simplified: A Practical Approach to the Early Diagnosis and Treatment of Neurologic Diseases Written Especially for General Practitioners and Students", by David Joseph Lafia, M.D.; 1960. Springfield, Illinois: Charles C. Thomas, Oxford: Blackwell Scientific Publications. 9" × 5¾", pp. 196, with illustrations. Price: 54s. (English).

"Diseases of the Nails", by V. Pardo-Castello, M.D., and Osvaldo A. Pardo, M.D.; third edition; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications. 8½" × 5¾", pp. 312, with illustrations. Price: 68s. (English).

"Relaxation for Childbirth", by Mary Barfield, M.Phys.A., with an introduction by Dr. Cyril Pink; 1960. London: William Heinemann Medical Books Ltd. 7¾" × 5", pp. 152, with illustrations. Price: 12s. 6d. (English).

"Clinical Gastroenterology", by F. Avery Jones, M.D. (Lond.), Hon. M.D. (Melbourne), F.R.C.P. (Lond.), and J. W. P. Gummer, M.S. (Lond.), F.R.C.S. (Eng.); 1960. Oxford: Blackwell Scientific Publications. 8¾" × 5¼", pp. 660, with illustrations. Price: 70s. (English).

"Trauma in the Aged", edited by Edgar M. Bick, M.D.; 1960. New York, Toronto and London: McGraw-Hill Book Company, Inc. 9" × 6", pp. 540, with illustrations. Price: $16.00.

"Man's Posture: Electromyographic Studies", by J. Joseph, M.D., M.R.C.O.G.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications. 9" × 5¾", pp. 98, with illustrations. Price: 44s. (English).

"The Management of the Doctor-Patient Relationship", by Richard H. Blum, Ph.D.; 1960. New York, Toronto and London: McGraw-Hill Book Company, Inc. 9" × 6", pp. 320. Price: $8.50.

"Principles of Medicine: An Integrated Textbook for Nurses", by James Verney Cable, M.D., M.R.C.P., F.R.A.C.P., with a foreword by Miss Flora Cameron, O.B.E., R.N., R.M.; 1960. Christchurch: N. M. Peryer Limited. 8½" × 5½", pp. 674, with 129 illustrations. Price: 55s. (New Zealand).

"Contributions to Obstetrics and Gynæcology", by V. N. Shirodkar, M.D. (Bombay), F.R.C.S. (Eng.), F.A.C.S.; 1960. Edinburgh and London: E. & S. Livingstone 9¾" × 6¾", pp. 167, with illustrations. Price: 37s. 6d. net (English).

"St. Peter's Hospital for Stone, 1860-1960", edited by Clifford Morson, O.B.E., F.R.C.S.; 1960. Edinburgh and London: E. & S. Livingstone. 9¾" × 7", pp. 70, with illustrations. Price: 21st net (English).

"The Urological Aspects of Bilharziasis in Rhodesia", by R. M. Honey, M.B., F.R.C.S. (Edin.), and M. Gelfand, C.B.E., M.D., F.R.C.P.; 1960. Edinburgh and London: E. & S. Livingstone Ltd. 8½" × 5½", pp. 80, with illustrations. Price: 7s. 6d. net. (English.)

"Obstetrical and Gynæcological Pathology for Post-graduate Students", by R. E. Rewell, M.D. (Lond.), M.R.C.P.; 1960. Edinburgh and London: E. & S. Livingstone Ltd. 8½" × 5½", pp. 448, with many illustrations. Price: 50s. net. (English).

"French's Index of Differential Diagnosis", edited by Arthur H. Douthwaite, M.D., F.R.C.P.; eighth edition; 1960. Bristol: John Wright & Sons Ltd. 10" × 6¼", pp. 1124, with many illustrations. Price: 126s. (English).

"Practical Birth-Control Methods", by Abraham Stone, M.D., and Norman E. Himes, Ph.D.; second edition; 1960. London: George Allen & Unwin Ltd. 8½" × 5½", pp. 208, with illustrations. Price: 21st net. (English).

"Textbook for Health Visitors", by Llywelyn Roberts, M.D., M.R.C.P., D.P.H., Beryl D. Corner, M.D., F.R.C.P., and C. H. Shaw, M.D., M.R.C.S., D.P.H.; second edition; 1960. London: Baillière, Tindall and Cox. 7¾" × 5", pp. 516, with illustrations. Price: 32s. 6d. (English).

The Medical Journal of Australia

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CHILDREN IN HOSPITAL AND PÆDIATRIC EDUCATION.

PURSUING the thesis that "even children are people" in these columns some years ago,[1] we quoted the comment on his aunt and uncle guardians made from the child's point of view by the narrator in Kenneth Graham's book "The Golden Age":

> They treated us, indeed, with kindness enough as to the needs of the flesh, but after that with indifference (an indifference, as I recognize, the result of a certain stupidity), and therewith the commonplace conviction that your child is merely animal.

The passage is devastating and one to ponder deeply, for the charge made by the child against the adult here is stupidity. Unfortunately, such a charge can all too frequently be sustained in a variety of circumstances, and not least in those pertaining to the medical and hospital care of children. It may be interjected that the subject has been discussed almost *ad nauseam*, and that everyone knows the position, or should know it. That is as may be, but the point is not easy to sustain when we have a highly responsible subcommittee of the Australian Pædiatric Association able to describe the purpose of a report prepared by them (see page 829) as being "to clarify the attitude of the Australian Pædiatric Association to two important questions affecting the total welfare of children, *in view of possible decisions of hospital and university authorities which might affect this welfare*". The italics are ours, but they are used to highlight the fact that adults can still be stupid. It is a matter for congratulation that the subcommittee has dealt with the situation clearly and vigorously and that the Australian Pædiatric Association has adopted the report, which brings forward constructive recommendations on the two important questions that it has to deal with.

The first part of the report, that on children in hospital, needs little comment. The subject is not new to these columns, and the subcommittee can quote ample support for its recommendations from both local and overseas sources. The essence of the recommendations is that the care of children should be provided in separate hospitals, blocks or wards in that order of preference. This offers the best provision for the child in specific medical and nursing care, in amenities and in personal environment, and should be adopted to the fullest extent that is feasible and appropriate in any particular community. Moreover, the principle behind it should not be allowed to break down; that is to say, children should only on the rarest occasions be admitted to adult wards, and then only for some reason related to their own interest, not the hospital's convenience. It is disturbing to be told that from time to time young children, the dependants of war widows, have been admitted to adult wards in repatriation hospitals in the company of hardened old soldiers and have, on discharge from hospital, known a lot more than when they were admitted. Surely the only reason for this sort of thing is some aspect of administrative convenience, and it cannot be accepted that this is more important than the welfare of the child. We hope that the Australian Pædiatric Association will adhere strongly to this principle and refuse to countenance any major departure from the recommendations that it has adopted.

On the part to be played by pædiatric teaching in a medical curriculum, the subject of the second part of the report, there is more room for difference of opinion. However, the recommendations in the report follow widely acceptable principles and should have general approval. They certainly adhere to the intention of promoting the total welfare of children, and they also recognize the major place of pædiatrics in medical practice and so its claim not only for a major place in the medical curriculum but also to integration into the over-all pattern of the curriculum. In a report issued in 1948,[2] a committee on medical education set up by the Council of the British Medical Association in England, under the chairmanship of Sir Henry Cohen, pointed out that pædiatrics was not a specialty in the usual sense; it was general medicine applied to a particular age period. However, it was desirable to teach it in a special course because it had special problems of its own. An important point made was that pædiatrics had a valuable contribution to make to the training of a good doctor.

> First, perhaps more than in any other part of the course, it helps to stress the preventive aspects of medicine, for pædiatrics includes in its scope the physical, mental and spiritual care of the child both in health and in disease, a charge fraught with great possibilities for good or for evil in childhood and adult life. . . . Secondly, in dealing with children the student learns with special force the value of history-taking and the need for careful clinical examination. Thirdly, no other part of his course serves so well to stimulate the development of those personal qualities which are essential in a good doctor, such as patience, gentleness, and kindness to the patient.

On the question of examinations, the B.M.A. report stated that the subject of pædiatrics must not be divorced in the mind of the student from general medicine as a whole; so the examination in pædiatrics should be closely linked with that in medicine. There was division of opinion in the B.M.A. committee on whether or not a separate examination in pædiatrics was desirable, but in neither case does there seem to have been any wish to regard pædiatrics as other than a major subject. Altogether, the B.M.A. report is in general accord with the Australian Pædiatric Association's recommendations, as are W.H.O. Technical Report No. 199 (cited in the subcommittee's report), the well-known Goodenough Report,[3] and the thoughtful statement on the subject by

[1] MED. J. AUST., 1952, 1: 225 (February 16).

[2] "The Training of a Doctor: Report of the Medical Curriculum Committee of the British Medical Association", 1948, Butterworth, London: 91.

[3] "Report of the Inter-Departmental Committee on Medical Schools", 1944, H.M. Stationery Office, London: 175-180.

Professor Allan Moncrieff made at the First World Conference of Medical Education in London in 1953.[4] Indeed, it is difficult to conceive of major disagreement from any informed source on the principles stated.

The one point stressed in most of these other reports but not clearly indicated in the Australian Pædiatric Association's recommendations is the importance of the preventive aspects of child health. We do not imagine for a moment that this omission reflects any lack of interest in this aspect of the subject on the part of the members of the subcommittee, and indeed it is probably implicit in certain phrases, particularly the term "child health". However, an explicit reference to it would round off what is otherwise an admirable short statement. We hope that the recommendations will claim the attention of all who are responsible for determining the place of pædiatrics in medical curricula in this country, and that they will lay them seriously to heart. If anything remains to be said on this subject, it is probably covered by the concluding paragraph of Professor Moncrieff's paper, which follows a reference to the importance of the resident pædiatric post for the newly qualified doctor in the latter part of his year of compulsory residency:

> The undergraduate medical student is now qualified and registered as a medical practitioner. Pædiatrics has played a material part in his training. It should now be abundantly clear that pædiatrics is *all* medicine and not a branch. Nevertheless the methods and difficulties associated with the age period involved make pædiatrics a special study. The advances and complications of the subject today necessitate physicians who devote their whole work to pædiatrics, but they remain general physicians in the field of internal medicine, often more general in their outlook and practice than many of their colleagues who confine themselves to one system in adults.

Current Comment.

LEUKÆMIA IN HIROSHIMA.

MUCH has been written about the effects of radiation on those who survived the events of August 6, 1945, in Hiroshima, both in scientific journals and in the popular Press. The publication of an authoritative report on leukæmia in Hiroshima atomic bomb survivors from the Hiroshima-Nagasaki Atomic Bomb Casualty Commission, a research agency sponsored by the U.S. Atomic Energy Commission and administered in cooperation with the Japanese National Institute of Health, is therefore a matter of considerable interest. This report appears under the names of a panel of seven American and Japanese investigators.[1]

In their introductory paragraph these authors point out that estimates of increased risk associated with exposure to radiation in man depend heavily upon studies of the survivors of the atomic bombing of Hiroshima and Nagasaki, and of patients with ankylosing spondylitis treated with high doses of X radiation; other clinical data on the effects of radiation in man are relatively scanty. They state that as regards the first group it is now possible to present analyses of incidence based on fixed samples of survivors; their report summarizes the findings observed in the Hiroshima survivors from 1945 to 1958. A similar report on the survivors of the Nagasaki atomic explosion is in course of preparation.

The best estimate of the population of Hiroshima at the time of the explosion is 225,000 persons, of whom 64,600 were killed and 72,200 injured. The survivors became widely dispersed, and three months later the population of the city was only about 42,000. Many others returned later, and today the population consists of a mixture of survivors and of recent immigrants to the city. The study of the incidence of leukæmia among survivors of the explosion is based mainly on the "Master Sample", which consists of the 90,000 exposed survivors enumerated by the Atomic Bomb Survivors Survey of 1950; of these, 97% have been traced. By the end of 1957 the Atomic Bomb Casualty Commission had knowledge of 130 persons exposed in Hiroshima who were said to have leukæmia, as well as 19 other cases of aplastic anæmia and leukæmia-related conditions; there were also a few cases of lymphoma, but these are reserved for a later report. Of the cases of leukæmia, 122 have been confirmed by members of the Commission, and these form the basis for their report.

Before proceeding to the analysis of their findings, the report draws attention to some general facts about leukæmia. The world-wide increase in the incidence of leukæmia in recent years is well known, and this has been noted both in America and in Japan. However, the increase in Japan has occurred only since the war, whereas in America it goes back to the 1930's, and it is thought that differences in likelihood of diagnosis do not account for these findings. A comparison of recent estimates of age-specific leukæmia rates in Japan with those observed in an American population centre shows that the incidence among young people of the two countries is very similar, but that among older people there is a much higher rate of leukæmia in the United States than in Japan. The high incidence of chronic lymphocytic leukæmia which is found among older people in the United States does not occur in Japan, where the recent increase in the incidence of leukæmia is primarily due to an increase in the number of cases of acute granulocytic leukæmia in the older age groups. There appears to be no doubt that these differences are real.

Analysis of the Commission's figures confirms the results of previous estimations that the incidence of leukæmia falls off sharply with increase in distance of exposed persons from the hypocentre of the explosion. It is not possible to be precise about the radiation dosage received by those nearest the hypocentre, because they owe their survival to the fact that they were to some extent sheltered by buildings, etc. However, calculations of air dosage show that this declined from 2620 rads at 800 metres from the hypocentre (a figure well into the supralethal range) to 20 rads at 2000 metres. The corresponding decline in the incidence of leukæmia is from 1720 per million *per annum* among those within 1000 metres of the hypocentre to 29 per million among those over 2000 metres from the hypocentre. The latter figure is not significantly greater than that reported for the population of Japan as a whole, and it is therefore concluded that there was no increase in leukæmia due to radiation exposure among those who were more than 2000 metres from the hypocentre at the time of the explosion. In spite of the impossibility of estimating the exact dosage received by persons exposed near the hypocentre, it is reasonable to assume that among those in Japanese-style timber houses at the time, the dose received would on the average have been proportional to the distance from the hypocentre. On this assumption it was possible to construct a graph relating incidence of leukæmia to exposure to radiation, and it was found that this relationship was linear over most of the range; it throws no light on the shape of the curve in the lower dose range. The question of the relation of the acute radiation syndrome to leukæmia is considered, but the results are inconclusive. The incidence of leukæmia is higher among those who developed acute radiation symptoms soon after the explosion than among those who had no such symptoms; but as the former group undoubtedly received a higher dose of radiation than those who showed no early signs of radiation sickness, all that can be said

[4] "Proceedings of the First World Conference on Medical Education, London, 1953, Held under the Auspices of the World Medical Association", 1954, Oxford University Press, London: 340.

[1] *Blood*, 1960, 15: 313 (March).

is that the incidence of leukæmia was raised in both groups, and that prior signs of severe acute radiation damage are therefore not necessary for the subsequent development of radiation-induced leukæmia. As regards the type of leukæmia encountered, chronic granulocytic leukæmia was the form most commonly observed, but the small number of cases made generalization difficult; the report states that it seems likely that all forms of leukæmia, with the possible exception of chronic lymphocytic and the Schilling type of monocytic leukæmia, are increased by exposure to ionizing radiation. At Hiroshima those who were over 60 years of age at the time of exposure have had an increased incidence of both acute and chronic granulocytic leukæmias; those who were then in the middle years of life have shown an increase mainly in the chronic granulocytic form; and those who were under 20 years of age at the time of exposure have shown an increase chiefly in acute unspecified types of leukæmia. The Hiroshima experience therefore differs in some respects from the results of British studies on the effects of irradiation for ankylosing spondylitis; these studies showed an increase primarily in the incidence of acute granulocytic leukæmia. The natural history of leukæmia in exposed survivors did not appear to differ from that of corresponding types of leukæmia in non-irradiated populations.

The question of the interval between exposure to radiation and the first appearance of cases of radiation-induced leukæmia is beset by the difficulty of obtaining accurate data for the years immediately after the war. No case of leukæmia among exposed survivors has been confirmed with onset before 1947: in the year 1947-1948 eight cases of leukæmia were confirmed, about twice what would have been expected in a non-irradiated population of the same size. Figures for the Master Sample are available only from 1950 onwards, and taken in conjunction with data from other sources these indicate that the incidence of radiation-induced leukæmia reaches its peak between four and eight years after exposure and thereafter declines, though even 13 years after exposure there was still evidence of an incidence of leukæmia slightly in excess of what would have been expected in a non-irradiated population. These findings agree broadly with the results of British studies on the incidence of leukæmia after exposure to therapeutic radiation for ankylosing spondylitis.

In the concluding paragraph of the report, two points are emphasized. The first is that in any given case only a presumptive relationship between radiation and leukæmia can be argued; leukæmia occurs in human populations with or without radiation exposure, and there is no way of distinguishing between that caused by radiation exposure and that occurring in non-irradiated persons. The second point is that, with the possible exception of low doses of radiation in utero, studies which have established a definite relation between radiation and leukæmia in man have without exception involved groups of people exposed to fairly large amounts of radiation. In spite of the considerable size of the popuiation involved at Hiroshima, the actual number of cases of leukæmia has been relatively small; these cases have been sufficient to provide answers to some of the first questions about the leukæmogenic effects of exposure to large doses of radiation, but they are quite insufficient to provide useful information about the likely effects of exposure to low doses. For this, further statistical studies are necessary of the effect of doses below about 50 to 100 rads; it may be a long time before agreement is reached about the possible effects of radiation in this range.

STEROIDS AND SURGERY.

IT is generally believed that corticosteroids are of proven value in the treatment of ulcerative colitis (favourable results from an extensive therapeutic trial were reported by S. C. Truelove and L. J. Witts in 1955),[1] but a recent surgical visitor to Australia, Professor J. C. Goligher, has reemphasized the surgical view[2] that such therapy may create many additional problems when and if surgery is performed. It is salutary, therefore, to see the recent study, albeit made retrospectively, by W. B. Ewart and J. E. Lennard-Jones[3] of the effects of corticosteroids on the surgical management of a group of patients suffering from ulcerative colitis, who were treated at St. Mark's Hospital, London. Ewart and Lennard-Jones compare the post-operative course, following a one-stage subtotal colectomy and ileostomy, of 131 patients operated on between 1951 and 1959. A patient is defined as being in the "steroid group" if he has received steroids at any time, in any amount, during the pre-operative year. The groups are further subdivided into four categories on the basis of the severity of the condition. It follows that Groups C and D, containing the more severely ill patients, are also those which have the highest proportion of patients in the "steroid group", a factor which makes interpretation of the post-operative course difficult. Consideration of the mortality figures shows that there were seven deaths (13%) in the steroid group and five deaths (6%) in the non-steroid. Among patients severely ill at the time of operation (Groups C and D), the mortality was approximately equal; 11 of the 12 deaths in the series occurred in these patients. The causes of death are familiar—post-operative circulatory collapse and peritonitis. The post-operative complications (defined as including even stitch abscesses) were equal in both groups, and there is no statistical justification in this series for suggesting that the degree of morbidity, as for example measured by days in hospital, was significantly modified by the steroid therapy. The remarks on bowel friability, a complication which has often been attributed to steroid management, are of special interest. A careful pathological examination of every colon removed in this series has revealed no difference between those patients receiving and those not receiving steroids before operation. In five cases the surgeon (or pathologist) had commented: "It tears like blotting paper", but only one patient was in the "steroid group". Ewart and Lennard-Jones summarize these findings by stating: "We can find no correlation between the pre-operative dose of corticosteroids and surgical result."

Need these conclusions cause much surprise? The findings of I. P. M. MacDougall[4] were very much the same, and although the steroids have been accused and shown experimentally in some instances to lower resistance to infection, delay wound healing and possibly predispose to venous thrombosis, the factual evidence in man for such complications while treatment is maintained on therapeutic levels is meagre and suspect. Even less acceptable data are available for the view that steroids given even a year previously render the patient susceptible to post-operative collapse. A much more reasonable view is that of Ewart and Lennard-Jones that the steroids are more effective in mild cases, causing a selection of only the very severe, complicated and advanced cases to be offered to the surgeon; hence the false reputation of the steroids. Looking at the problem from the other side, we may ask if the corticosteroids have a positive contribution to make towards surgical safety. They probably have. There is much evidence to support the view that even the severely ill patient is temporarily benefited by steroids. This amelioration is, however, short-lived, and if no improvement occurs, they should not be persisted with. Their place is definable, therefore, as a pre-operative treatment to bring the patient in the best possible condition to the surgeon. It is reasonable to suggest that no seriously ill patient with ulcerative colitis, except for acute complications, should be submitted to surgery unless vigorous medical treatment, including administration of steroids, has first been applied. As in many other fields of gastro-enterology the best results follow close and intimate collaboration between surgeon and physician.

[1] *Brit. med. J.*, 1955, 2:1041 (October 29).

[2] *Scot. med. J.*, 1959, 4:1 (January).

[3] *Lancet*, 1906, 2:60 (July 9).

[4] *Proc. roy. Soc. Med.*, 1959, 52 (Suppl.): 9.

Abstracts from Medical Literature.

RADIOTHERAPY.

Wilms's Tumour.

H. J. KLAPPROTH (*J. Urol. (Baltimore)*, May, 1959) reports that 45 cases of Wilms's tumour have been treated at the Cleveland Clinic from 1921 to 1958, and also presents an analysis of 1351 cases reported in the world literature over the period 1940 to 1955. Wilms's tumour accounts for 20% of all malignant tumours of childhood; the incidence of Wilms's tumour in the adult is low, but it does occur as late as the eighth decade. The symptoms, signs and radiological findings are discussed. The over-all cure rate in the large series is 20% to 27%, though some authors report a cure rate as high as 47%. Nephrectomy alone gave 20% of cures, pre-operative irradiation and nephrectomy 27%, nephrectomy and post-operative irradiation 26%, and pre-operative irradiation, nephrectomy and post-operative irradiation 24% in the total of 1351 patients. It is noted that patients treated prior to the age of one year have a better prognosis than those in the older age group. Those patients who survive the first post-operative year have a good prognosis, as 85% of those who died did so during the first year. The prognosis after two years is good, and those patients without recurrence after three years can be regarded as cured. The author concludes that radiotherapy should be given in every case.

Incidence of Neoplasia after Thymic Irradiation.

H. B. LATOURETTE AND F. J. HODGES (*Amer. J. Roentgenol.*, October, 1959) present a report on 958 patients who had the thymic region irradiated during the 20-year period ending in 1951. The dosage was low, less than 150*r* in 122 cases, most patients (661) receiving between 150*r* and 200*r*. Information on 867 is given, of which group 99 are dead. Two developed lymphoblastoma, one leukæmia, and one lymphosarcoma. This incidence is slightly higher than might be expected in an unirradiated population, but not significantly so. One patient developed thyroid carcinoma. The authors state that these findings are suggestive of some increase in the incidence of neoplasia after irradiation of the thymic region.

Transsphenoidal Destruction of the Hypophysis.

R. D. MOSELEY, JR, *et alii* (*Amer. J. Roentgenol.*, October, 1959) discuss their experience in the use of radioactive yttrium for the destruction of the pituitary gland. A modified 17-gauge spinal needle is passed into the pituitary fossa using a portable image intensifier and some 6 to 11 pellets are inserted. Fifty patients have been treated this way, including seven males (six with prostatic carcinoma and one with breast carcinoma). Of the 42 patients with carcinoma of the breast there has been subjective or objective benefit in 22 patients. Of the six males with carcinoma of the prostate, there was improvement in four; two patients with carcinoma of the ovary were treated, but without benefit. It is pointed out that hypophysectomy will produce palliation in cases of endocrine-sensitive tumours, and this method, in contradistinction to surgical ablation, has been without mortality. There are, however, complications. These were: extraocular palsies in 18 cases, cerebro-spinal rhinorrhœa in 12, and meningitis in 6.

Potential Radiosensitizing Agents.

D. H. MARRIAN (*Brit. J. Cancer*, September, 1959) reports the results of a study of some of the biochemical processes affected by "Synkavit". Mice suffering from Ehrlich mouse ascites tumour were injected with 2 mg. of "Synkavit" and with C^{14}-labelled formate or glycine, and the uptake was studied in the purines of the tumour over a two-hour period; "Synkavit" was omitted from a control group. It was shown that "Synkavit" reduced by 20% to 25% the uptake of precursor into RNA, but did not alter uptake into the purines of the acid-soluble nucleotides or into DNA. The action of "Synkavit" as a radiosensitizer may therefore involve interference with RNA synthesis while the X ray is interfering with DNA synthesis, and this two-pronged attack on the cell's functions may account for the more than additive effect of combined treatments.

Carcinoma of the Base of the Tongue.

V. A. MARCIAL (*Amer. J. Roentgenol.*, March, 1959) states that in Puerto Rico carcinoma of the base of the tongue is the most frequently encountered tumour in the oral and pharyngeal cavities, including the lip. A series of 240 cases is presented and of these 208 patients had developed metastases in the cervical area at the time of admission to hospital. In view of this, the prognosis was poor, and the five-year survival rate in this series is 11%. Most of these patients have been treated by external supervoltage radiation with the occasional use of radium and radon seeds. The author considers that even when the whole tongue is involved treatment gives good palliation and prolongation of life.

RADIOLOGY.

The Acromio-Humeral Distance in Health and Disease.

C. ALEXANDER (*Proc. Coll. Radiol. Aust.*, December, 1959) has noted that the distance between the acromion and humeral head is, in health, fairly constant. In diseased shoulders, on the other hand, this distance is not infrequently diminished, sometimes with associated bony degenerative changes, sometimes without other evidence of disease. The space between the humeral articular surface and the acromion is occupied mainly by the supraspinatus tendon and capsule. The articular cartilage and bursa contribute less than one-third. It is unlikely that spasm could compress these structures significantly and any reduction in distance can reasonably be interpreted as indicating rupture or more commonly degenerative attrition of the supraspinatus tendon. The author concludes that reduction of the acromio-humeral distance below 7 mm. is a reliable indication of degenerative changes in the supraspinatus tendon/subdeltoid bursa complex. The evidence is strengthened if degenerative changes are present in the tuberosity or if there is definite faceting of the acromion. If X-ray films have been taken of both shoulders, a difference between the two sides further strengthens the evidence. The only sources of error are centring too low, so that the acromion is not profiled, or measuring to the tuberosity instead of the articular surface. Conversely, any increase of the distance above 13 mm. is likely to indicate either bursitis or traumatic subluxation.

Renal Puncture as a Diagnostic and Therapeutic Procedure.

A. C. BEGG (*Proc. Coll. Radiol. Aust.*, December, 1959) describes the method of examination and indicates the value of renal puncture as a diagnostic and therapeutic procedure. He states that the chief reasons why this method has not been practised widely stem from the potential hazards of disseminating a neoplastic lesion or of spreading hydatid disease by the needle puncture. If cases are wisely selected neither of these theoretical hazards is likely to be encountered. The accuracy of diagnosis compares more than favourably with other diagnostic procedures. In the author's experience a correct diagnosis was made in every case except one—the error here lying in the interpretation of inexperience. While, on occasion, a neoplasm may develop in a cyst and a cyst may occur in a neoplasm, or both may be present in different parts of the same kidney, the injection of contrast medium at the time of the puncture enables the distinction to be made. In a high proportion of cases puncture of the cyst with aspiration leads to cure.

Distinction between Crohn's Disease of the Large Intestine and Ulcerative Colitis.

H. E. LOCKHART-MUMMERY AND B. C. MORSON (*Gut*, June, 1960) describe and illustrate 25 cases of Crohn's disease (regional enteritis) of the large intestine. They point out that most of this series of patients had had a barium enema examination carried out at some time, and many of them had also had a barium meal and follow-through examination. The radiological appearances naturally depend on the distribution and severity of the disease. Ulcerative colitis is a disease that nearly always extends in continuity, and the appearance of scattered areas of disease separated by normal parts is very suggestive of Crohn's disease, as is also the appearance of localized strictures of the bowel. Disease that is more severe on the right side of the colon than on the left is more likely to be Crohn's disease than ulcerative colitis. Reflux of a barium enema through the ileo-caecal valve which demonstrates narrowing of the terminal part of the ileum as well as an abnormal colon suggests Crohn's disease, as the terminal ileum which becomes involved in the retrograde spread of ulcerative colitis is characteristically

dilated. The authors point out that in many of these cases a diagnosis of ulcerative colitis or tuberculosis was made at some time during the illness, and often the correct diagnosis was not apparent until the bowel had been removed and the histology studied. However, they believe that, with increasing experience, cases presented at their hospital in recent years have in several instances been correctly diagnosed before operation, and that in many cases the diagnosis can be established on clinical and radiological grounds, aided when possible by biopsy.

The Radiological Diagnosis of Asbestosis.

R. WILLIAMS AND P. H. JONES (*Thorax*, June, 1960) describe a study which was made in order not only to determine the specificity of the radiological changes in asbestosis but to see to what extent their diagnosis and grading were affected by observer variability. There were several surprising findings in this study. One was the extent of the disagreement between the observers in the diagnosis of films from certified cases of asbestosis. These patients had all been seen and certified by the pneumonoconiosis medical panels and their films had initially been selected by the authors as typical examples of the disease. Yet when the same films were viewed in the present trial the number thought to show changes consistent with the diagnosis of asbestosis varied from 40% to 80% according to the observer. If the industrial history or physical signs of these patients had been known, many of the films regarded as abnormal but not examples of asbestosis would have been correctly diagnosed; however, the question was not whether the patient did or did not have asbestosis, but whether the changes seen in the radiographs were consistent with this diagnosis. All observers had special experience in this field, and with one exception had little difficulty in diagnosing the films from normal subjects. It is clear that little reliance can be placed on the presence of radiological changes in the diagnosis of early cases of asbestosis. It is also apparent that the radiological appearances in asbestosis are by no means specific, and may be confused with such widely differing diseases as chronic bronchitis and emphysema, sarcoidosis, and other pneumonoconioses. If examples of other interstitial fibroses such as scleroderma, lymphangitis, carcinomatosis, xanthomatosis or beryllium granuloma had been included in this group, the confusion would presumably have been even greater.

Fracture of the Carpal Navicular.

OTTO RUSSE (*J. Bone Jt Surg.*, July, 1960) states that if there is tenderness in the region of the navicular, a fracture of this bone should be suspected, especially if this sign develops after a fall on the dorsiflexed hand or a blow on the palm with the wrist in dorsiflexion. In such cases it is considered preferable routinely to take the following skiagrams: (i) a dorso-volar view, with the forearm in neutral position mid-way between pronation and supination and the wrist in slight dorsiflexion with the fingers closed into a fist; (ii) a similar view, with the forearm in 15° to 20° of supination; (iii) a true lateral view with the forearm in 90° of supination; (iv) a dorso-volar view, with the forearm in 15° to 20° of pronation. Ulnar deviation of the wrist while these skiagrams are made should not exceed 10° with fresh fractures, to avoid distraction of the fragments. In the presence of pain without definite X-ray findings, even when the film is studied with a magnifying glass, the recommended procedure is to apply a cast for two weeks and then repeat the film. Should tenderness on pressure or pain on wrist movement persist at this time, even to a slight degree, the wrist should again be immobilized, and the X-ray examination repeated after a further two weeks. Fissured fractures of the navicular occur that can be demonstrated only after three to four weeks, when absorption has widened the fracture cleft. About 70% of navicular fractures are located in the middle third, 20% in the proximal third, and 10% in the distal third of the bone. Since most of the blood vessels enter the navicular in the distal part (the tuberosity) and on the dorsal aspect of the middle part (the waist) of the bone, the conditions for healing are better with fractures in the distal and middle thirds. Therefore, the average time necessary for bone union to occur is longer for fractures in the proximal third, in which the time amounts to 10 to 12 weeks, than for most fractures in the distal and middle thirds, for which six to eight weeks of immobilization is necessary. Immobilization in fractures of the navicular should be continued until the X-ray films show definite signs of bone union. In the absence of clearly visible osseous trabeculations bridging the former defect, one should look for increased density of the bone at the site of the former fracture cleft or on each side of the cleft. These calcified bands in the fracture site or on both sides of the fracture site are signs of bone union in fresh fractures of the navicular. Such calcification occurs in about 40% of fresh fractures. In old fractures, these bands cannot be considered as signs of bone union.

Intravenous Cholangiography in Acute Cholecystitis.

H. C. JOHNSON, JR, *et alii* (*Radiology*, May, 1960) state that intravenous cholangiography has found widespread application in the recognition of a variety of chronic biliary tract disorders. The authors discuss use of this procedure in the recognition of acute cholecystitis and describe the results of emergency intravenous cholangiography in 220 patients seen with acute abdominal signs and symptoms. The group included 69 patients with proved acute cholecystitis. It is commonly accepted that cystic duct obstruction, whether due to calculus or inflammation, is an essential feature of acute cholecystitis. If that premise is accepted, it should prove impossible to visualize the gall-bladder during an attack of this disease. On the other hand, in acute abdominal illnesses other than cholecystitis the absence of cystic duct obstruction should allow gall-bladder visualization, provided hepatic excretion of intravenously administered "Biligrafin" is adequate. Demonstration of the presence or absence of cystic duct obstruction was therefore the objective of this study. The authors' experience to date indicates that, once visualization of any segment of the biliary duct system is accomplished, ensuing X-ray films will allow direct demonstration of this phenomenon. When biliary duct visualization was obtained in acute clinical disorders other than acute cholecystitis (this occurred in two-thirds of this group) visualization of the gall-bladder invariably followed. On the other hand, the duct system was visualized in 47% of patients with acute cholecystitis, and in none of these was the gall-bladder visualized. Gall-bladder visualization therefore reliably excluded the existence of acute cholecystitis in this series of patients. These findings lend support to the concept that cystic duct obstruction is an essential feature of this disease. The greatest potential source of error lies in concluding that cystic duct obstruction is present when X-ray films have been obtained for only one or two hours after injection. When duct visualization occurs in excellent concentration on early films, a diagnosis of cystic duct obstruction is warranted if technically adequate radiographs fail to show gall-bladder opacification within two hours. If, however, the initial duct visualization is of less than excellent density, or if the subsequent X-ray films are of unsatisfactory quality, additional delayed films are essential. A four-hour post-injection film has been found adequate for this purpose. When in doubt, a diagnosis of cystic duct obstruction should be deferred until a four-hour X-ray film of good quality has been viewed.

The Stomach and Duodenum in Carcinoma of the Pancreas.

H. CHIAT AND D. H. FAEGENBURG (*Radiology*, May, 1960) state that certain cases of pancreatic cancer may be radiographically indistinguishable from primary cancer of the stomach. The symptoms experienced by the patients in the author's series are similar to those observed in much larger series of patients suffering from gastric neoplasms. Abdominal masses are commonly felt in both diseases. Standard laboratory procedures are of little differential value. Anæmia is frequent in both gastric and pancreatic cancer. Traces of blood in the stool are not always indicative of a mucosal lesion. Several patients had guaiac-positive stools despite the absence of mucosal involvement. Moderate elevations of serum bilirubin and alkaline phosphatase levels shed little light on the problem, as these values may be elevated in the presence of liver metastases from any source. Frank jaundice favours a diagnosis of carcinoma of the head of the pancreas. Only one patient was clinically jaundiced, and this occurred while he was undergoing study in the hospital. Absence of hydrochloric acid in gastric secretions is of little specificity; four patients in the series discussed had histamine-fast achlorhydria. These patients were of an age group in which achlorhydria is common. The authors conclude that a radiographic picture of carcinoma of the stomach, when challenged by a negative result of cystological examination, should alert the observer to the possibility of a primary pancreatic neoplasm.

Medical Societies.

AUSTRALIAN PÆDIATRIC ASSOCIATION.

THE annual meeting of the Australian Pædiatric Association was held on April 22 to 25, 1960, at Canberra, DR. H. MCLORINAN, the President, in the chair. Part of the report of this meeting appeared in the issue of November 12, 1960.

Myelomeningocele.

E. DURHAM SMITH (Melbourne) read a paper entitled "The Pathogenesis and Management of Myelomeningocele" (see page 801).

T. Y. NELSON (Sydney) said that in Sydney the management of such cases in general was substantially along the lines laid down by Mr. Durham Smith. Until recently he had followed the school of thought which laid down that operation should be postponed until the age of 12 months, but now he considered that that was delaying operation too long. He did not think that a meningocele should be operated on if hydrocephalus was obvious at birth. His own practice was to defer the decision about operation until the infant was about three months old. By that time many of the cases had been eliminated, and the spinal mass was nearly always covered by a healed surface. He asked whether it was harmful to remove the mass of proliferated nervous tissue which was sometimes found.

Mr. Durham Smith replied that that was an extremely difficult question to answer. He himself usually lacked the courage to remove that tissue, but at the same time really doubted whether it was worth preserving. Likewise he doubted whether the peripheral roots were worth preserving, for although they were certainly conductive, as one could see by placing an electrode on them, they did not have functional connexions with the dysplasic cord mass.

J. STEIGRAD (Sydney) said that he had always preferred to operate on the back early for cosmetic reasons and because of the difficulty of caring for affected children at home. The entrance of such an infant to the home made a most unpleasant impact on the whole family unit. He asked what placement was possible for those infants for whom operation was not indicated.

Mr. Durham Smith agreed that the placement of such infants constituted a great problem. Some could be placed in institutions, but the majority simply had to go home, although that was clearly undesirable in many cases.

D. MCKAY (Adelaide) asked whether the dorsal roots were histologically normal, and whether the absence of movement below the hips and the presence of patulous sphincters influenced the decision to operate.

Mr. Durham Smith replied that the microscopic appearance of the nerve roots was the subject of a continuing investigation, but his preliminary findings were that they were probably normal. He did not consider the neurological state a factor that entered into the decision to operate. That might seem a surprising statement; but his whole thesis was that some of those infants would survive irrespective of what action was taken, and responsibility had to be accepted for them in any case. The neurological state was therefore irrelevant to the question of whether treatment should be undertaken.

C. WALKER (Sydney) asked whether the siblings were affected in many cases.

Mr. Durham Smith replied that of 179 families there was an affected sibling in 7·8%. In a further 6·8% of the families there was another sibling with a congenital anomaly other than myelomeningocele.

Experiences with Actinomycin D Chemotherapy.

J. COLEBATCH (Melbourne) read a paper entitled "Experiences with Actinomycin D in the Treatment of Malignant Disease in Children" (see page 804).

ALAN WILLIAMS (Melbourne) said that the secondary deposits of malignant tumours of childhood were usually less differentiated than the parent growth. Microscopic study of the sections of metastatic deposits in some of the treated cases showed a variety of mature tissue; he regarded that as a very hopeful sign.

N. A. A. MYERS (Melbourne) said that 26 patients with Wilms' tumour had been admitted to the Royal Children's Hospital, Melbourne, in the ten-year period from 1945 to 1955; 23 subsequently died. Since then there had been a further 20 patients, 11 of whom had died. The majority of recent survivals had received chemotherapy, usually actinomycin D. It had been decided in 1959 to divide all cases of Wilms' tumour into four groups, the most important and largest group comprising those cases in which there was no clinical or radiological evidence of metastasis. The policy was to operate on those patients under a cover of actinomycin D and to follow it with the ordinary radiotherapeutic régime. In those cases in which metastasis had already occurred, he thought that surgery had a lot to offer. The combined surgical and chemotherapeutic approach would make a significant difference to the results obtained in the treatment of Wilms' tumour.

S. W. WILLIAMS (Melbourne) said that if the same critical approach that obtained in the chemotherapy of infectious disease was used in the chemotherapy of malignant disease, then very few of the drugs under discussion would be used on human beings. He thought that family attitudes could easily be taken as an excuse for the use of chemotherapy, when that line of treatment was not really justified. Whilst appreciating the work being done on the subject, he stressed that care should always be taken that harmful procedures were not carried out on children unless really good results could be anticipated. He thought that chemotherapy was still a long way from providing definite hope in such cases.

E. S. STUCKEY (Sydney), in differing from Dr. Stanley Williams, said that he regarded it as definitely established that the chemotherapy of malignant disease in childhood had in fact justified itself. Even quite radical measures were justified if time showed that some of the patients would have died without them.

DOUGLAS COHEN (Sydney) said that he strongly disagreed with the views of Dr. Stanley Williams. For too long the outlook on malignant disease in childhood had been coloured by experience with malignant disease in adult life. The situation was not the same; it could not be too strongly emphasized that malignant disease in childhood tended to be one of remission and relapse. He held that they were at the dawn of a successful biochemical or humoral attack on childhood cancer.

Massive Chemotherapy for Malignant Disease in Childhood.

DOUGLAS COHEN (Sydney) read a paper entitled "Massive Chemotherapy for Malignant Disease in Childhood" (see page 807).

The Intestinal Mucosal Lesion in Cœliac Disease.

CHARLOTTE ANDERSON (Melbourne) read a paper on the intestinal mucosal lesion in cœliac disease, in which she presented the results of a histological study of the duodenal mucosa in affected patients. The specimens of mucosa were obtained by biopsy with a peroral tube. Dr. Anderson said that until recently it had been thought that there were no structural alterations in the intestine in that disease, any changes that had been seen being attributed to post-mortem spoiling. During recent years it had become possible to take biopsy specimens of the small intestinal mucosa by a tube passed by mouth, and several groups of workers in England and America had shown that in patients with adult idiopathic steatorrhœa definite abnormalities were seen in the mucosa of the duodenum and jejunum. Similar changes had now been demonstrated in cœliac disease, firstly by Shiner and Doniach of Hammersmith, and then by Rubin of Seattle. The changes appeared to be consistently present in untreated cœliac disease, but to vary in severity. Whether they altered, improved or disappeared during treatment on a wheat gluten-free diet had not been clearly demonstrated, but both those workers had expressed doubts that the lesion was reversible.

Dr. Anderson demonstrated by slides the type of lesion and its variations in a group of newly-diagnosed cases of cœliac disease. She then showed the progress of the lesion after treatment in several of the cases. She said that duodenal biopsies had been obtained from 17 patients with cœliac disease, and 11 of them had been subjected to serial biopsy during treatment. Diagnosis had been made according to rigid criteria, such as the typical clinical history, a physical examination, the presence of steatorrhœa revealed by fat balance, a normal response to the sweat test, normal duodenal enzymes and good subsequent clinical response to a wheat gluten-free diet. The biopsies had been obtained with a Rubin-type tube. The tube was manœuvred into the duodenum under image-intensifier-television fluoroscopy, the child being under basal anæsthesia with "Brometh" given by the rectum. Biopsy specimens obtained were 3 to 4 mm. in length, and consisted of mucosa and muscularis mucosæ with a minimum of submucosal tissue. No post-biopsy difficulties had been experienced.

The changes seen in the duodenal mucosa included the following: flattening of villi and reduction in their number; a relative increase in the thickness of the tunica, with infiltration of plasma cells, small round cells and eosinophils; alteration in the surface layer of columnar cells, in that they were flattened and irregular or replaced by several layers of elongated cells, almost stratified in appearance. Goblet cells appeared to be reduced, and crypts appeared to be increased in length. In all 17 cases most of those changes were seen, although they varied in severity. The variation showed little correlation with the age of the child or the severity of the clinical symptoms. Two of the children, who were aged 18 months and had shown symptoms for only about two months, showed the least severe changes. In their specimens villi were flattened, but surface columnar cells were not altered to such an extent as in the other 15 patients. However, among the others, even children aged 18 months showed severe changes. Two boys aged 10 years showed complete absence of villi and markedly changed surface cells.

Dr. Anderson then showed slides of the biopsy specimens of four of the 11 children who had been followed during treatment. Each time the biopsy was repeated, a three-day fat-excretion test was done, and hæmoglobin value and weight gains were recorded. All of the 11 had shown improvement in the appearance of the mucosa when their biopsies were repeated either three months or nine to 12 months after the institution of treatment. The degree of improvement again was not consistent and did not correlate closely with the clinical condition, but did correlate more closely with the strictness of the gluten-free dietary régime. Five children had follow-up biopsy specimens which approached normal in appearance. On the whole, the villi were not quite so numerous or so long and finger-like as in several normal control specimens which were shown. However, the surface epithelium had resumed its normal appearance, goblet cells were normal in number and character and the tunica had become thinner and did not show an abnormal infiltration with cells.

Five children showed a lesser degree of improvement, in that the villi were still somewhat reduced with flattened tips, but surface cells were in good condition. One child, who had not been carefully dieted at all owing to social factors, showed the least improvement, although she had provided one of the less severely abnormal original biopsies.

Dr. Anderson said that she considered that the lesion was reversible. It was extremely hard to know whether a diet was quite free from gluten, and ingestion of very small amounts of the substance did not result in clinical upset. However, it was probably hard to expect absolute normality in the bowel unless all traces of gluten were removed from the diet. She held that her results had shown great improvement in the appearance of the mucosa, indicating at least that the changes were not the primary lesion, but were in some way induced by the presence of wheat gluten in the diet. The mechanism was still unknown, but she said that the availability of biopsy material had opened up a field of intracellular enzyme studies of the bowel mucosa, and work along those lines was being carried out in the Clinical Research Unit of the Royal Children's Hospital, Melbourne.

HATTIE ALEXANDER (U.S.A.) said that Dr. Anderson's paper provided a convincing demonstration of an hypothesis which had been widely advanced, but questioned by some. She asked whether it was likely that, in a patient whose intestinal mucosal pattern had reverted to normal under treatment, it would be likely to relapse into the abnormal pattern described if gluten was reintroduced into the diet.

Dr. Anderson replied that that information was not yet available.

Experimental Hyperparathyroidism in the Rat.

DONALD B. CHEEK (Melbourne) read a paper on experimental hyperparathyroidism in the rat. He made some general remarks concerning the rôle of the parathyroids in disease. The function of the parathyroid gland in controlling the equilibrium between extracellular calcium concentration and the calcium of the bone was emphasized by demonstrating experiments on parathyroidectomized rats. Similarly the action of parathyroid extracts on urine phosphorus, sodium and chloride of normal rats was shown. Mention was then made of the condition of parathyroid hyperfunction and the symptomatology that arose from it. The condition of parathyroid hormone intoxication was induced in rats and the changes in muscle electrolyte and bone electrolyte and nephrocalcinosis were demonstrated. The effect of varying the diet and magnesium intake was particularly emphasized, as also was the deleterious effect of magnesium loading. It was suggested that for patients in parathyroid hormone intoxication (i) loss of electrolyte (sodium chloride) explained some of the symptoms, (ii) the nature of the mineral intake of the food might be important therapeutically (especially to bone changes) and (iii) magnesium loading would aggravate the whole situation.

Dr. Cheek said that the work had recently been published in full (Cheek, D. B., and Teng, H. C., *Clinical Science*, February, 1960).

PROFESSOR W. B. MACDONALD (Perth) said that in inducing experimental hypercalcæmia in rats by the use of vitamin D, he had found that renal calcification occurred in an unpredictable fashion. He asked whether the diet in terms of magnesium had any effect on the calcification induced by vitamin D. He said that he had recently had a child who had presented with rickets and was found to have idiopathic renal acidosis, with a slightly raised blood urea level but with a very low serum phosphate level. He presumed that she had secondary hyperparathyroidism. With treatment she improved, but the blood urea level did not fall as much as he would have liked. Dr. Cheek's paper seemed to indicate that in a case like that, attention to the diet would be of the utmost importance in minimizing renal damage. As magnesium was present in both animal and vegetable foodstuffs, he could not see how satisfactory dietary control could be achieved.

Dr. Cheek replied that he did not use vitamin D in his experiments, but the calcification which he had found in his different groups of experimental animals had actually occurred in clear-cut fashion. He did not know what effect the addition of vitamin D would have had. He had always thought that there was a change in magnesium metabolism in so-called idiopathic hypercalcæmia, a condition which was believed to be related to increased sensitivity to vitamin D. In answer to Professor Macdonald's second question, Dr. Cheek said that during acute parathyroid hormone intoxication, magnesium was highly deleterious; that had been observed clinically. With chronic hyperparathyroidism, however, he did not think that magnesium would have any ill effect, although the magnesium intake of the diet of patients with hyperparathyroidism was an important matter. He agreed that they would have to be given a very odd diet in order to minimize magnesium intake, and he did not know how that could be achieved.

The Incidence of Infection following Splenectomy in Childhood.

MARGARET HORAN (Melbourne) read a paper entitled "The Incidence of Infection following Splenectomy in Childhood" (see page 809).

A. RIGG (Sydney) said that he had been conducting a similar study in Sydney, which was still incomplete. Fifty-six cases had been extracted from the records of the Royal Alexandra Hospital for Children in Sydney for the period 1943 to 1958, and although all those patients had not yet been followed up, four children had so far been found to have died. Three of the deaths had been due to the primary condition for which the splenectomy had been performed—for example, gastro-intestinal hæmorrhage in a child with portal hypertension. A boy, aged thirteen and a half years, had died from pneumococcal septicæmia four years after a splenectomy. His spleen had been removed because of chronic splenomegaly of five years' duration, the spleen showing chronic hypertrophic fibrosis of indeterminate ætiology. Dr. Rigg emphasized the lack of reports of serious infection in children whose splenectomy had been performed for traumatic rupture. McKinnon *et alii* had reported 26 such cases in which follow-up investigation had not disclosed any severe infection. He thought the spleen was still as Galen had described it—an organ full of mystery. However, it was apparent that in young infants splenectomy did seem to carry the hazard of subsequent severe infection. All pædiatricians should be aware of that hazard, and it was important that any infection in the splenectomized child should be promptly and vigorously treated.

HATTIE ALEXANDER (U.S.A.) said that Dr. Horan's excellent clinical analysis had been needed for some time, in order to make pædiatricians think objectively about the problem, and to assess the many published papers. It had been suggested that the underlying condition played a role in the production of subsequent infection, and Dr. Horan had suggested a possible explanation of that—namely, that the treatment given was responsible. That was the case in patients suffering from Cooley's anæmia, who had been shown by Dr. Smith to contract pneumococcal infection frequently, the cause of which was probably related to the many transfusions those patients received. Dr. Alexander thought that perhaps the absence of the spleen *per se* was

not the cause of the infections, but rather medical carelessness in the giving of intravenous infusions.

R. FOWLER (Melbourne) said that he was interested in the subject because of his work in tissue transplantation and mammalian recovery following total body-irradiation. One of the greatest risks to the irradiated patient was death from infection in the early post-radiation period. Animals could be protected against that by injections of bone marrow or of spleen cells, and there was evidence to suggest that spleen cells were more effective than bone marrow in that regard. One reason was that bone marrow was very slow to repopulate the lymph nodes, thymus and spleen of the irradiated animal. Spleen cells, on the other hand, very rapidly repopulated those tissues. If bone marrow from animals previously stimulated with an antigen was used for subsequent protection against lethal radiation, the immunological response in terms of measured antibody production was very inefficient. However, if spleen cells were used, antibody production was rapid after restimulation. One could theorize from this that if the spleen was removed, an individual was then entirely independent of bone-marrow mechanisms for immunological defence; if underlying disease was present, then those patients might well be worse off. Although Dr. Horan had been hesitant to draw conclusions from her figures, he thought that they contained a strong suggestion that underlying disease of the bone marrow was important, and he felt convinced that, at any rate in children, such disease constituted a serious hazard if splenectomy was undertaken.

Childhood Hepatic Cirrhosis.

S. T. ACHAR (Bombay) read a paper entitled "Some Problems Connected with Childhood Hepatic Cirrhosis" (see page 810).

An Unusual Case of Phenylketonuria.

IAN C. LEWIS (Perth) presented a paper entitled "An Unusual Case of Phenylketonuria" (see page 811).

FELIX ARDEN (Brisbane) said that he had had a similar experience, although by persisting with the treatment his patient had begun to improve after the first three months of life. Whatever might be the cause of the young infant's failure to thrive on orthodox diets of low phenylalanine content, he felt no enthusiasm about "Cymogran" as a food for babies.

Dr. Lewis agreed, and pointed out that the patient under discussion had required tube feeding.

M. J. ROBINSON (Ballarat) wondered whether acidosis might have played a part in the patient's poor progress, and inquired whether electrolyte estimations had been carried out.

Dr. Lewis replied that those estimations had given findings within normal limits, and that the patient had been at no time acidotic.

J. H. COLEBATCH (Melbourne) asked on how substantial a basis rested the figures for blood phenylalanine levels that were currently accepted as being permissible.

Dr. Lewis replied that he used the levels laid down by Payne *et alii*, but did not think they were necessarily strictly applicable to every case, and in fact he had allowed considerably higher levels in the case presented.

Unilateral Renal Disease with Hypertension.

FELIX ARDEN (Brisbane) read a paper entitled "Unilateral Renal Disease with Hypertension" (see page 813).

PETER GRANT (Brisbane) read a paper entitled "Unilateral Renal Disease with Hypertension in Children: Surgical Aspects" (see page 814).

A. M. CLARKE (Melbourne) said that it was important that the diagnosis should be made early and treatment carried out before the effects of hypertension became irreversible. He added that trauma sometimes produced unilateral renal damage; it was important that children in whom that had occurred should be followed up for some time, so that if hypertension developed nephrectomy could be performed at an early stage.

D. B. CHEEK (Melbourne) said that in patients with unilateral renal disease and hypertension there was a great need for investigation of sympathetic activity. In many cases there was an increased response to injected epinephrine. Improved methods had recently become available for assessing what rôle if any the adrenal medulla played in those cases. The presence of normal renal tissue was of great importance, although just how it produced its effects was obscure. Experimental work in Texas had shown that when renal tissue was seeded into the lungs of hypertensive dogs, the blood pressure returned to normal. Similarly studies with twins had shown that transplanting a normal kidney from one twin to another twin who had bilateral renal disease caused the blood pressure to fall in the latter, even though the damaged kidneys were not removed.

F. D. STEPHENS (Melbourne) said that Dr. Dora Bialestock had investigated that problem in Melbourne, but he thought that she had found only seven cases in 15 years of unilateral renal disease causing hypertension. In two of those cases the damage had been caused by trauma, and microscopic examination of sections had shown considerable hypertrophy of the cells of the adrenal medulla.

G. WESTLAKE (Melbourne) asked whether it was feasible to carry out partial nephrectomy in that type of case.

Mr. Grant replied that, although some normal tissue had apparently been present in the kidneys he had removed, the kidneys themselves had been very small, and any attempt at partial nephrectomy would not have been justified. The procedure might be worth while in a case in which an arteriogram showed an abnormal artery going to one segment, but as a rule the procedure was not justified.

D. COHEN (Sydney) said that Mr. Grant's paper emphasized the necessity of renal angiography in cases of suspected unilateral renal disease. It was advisable to expose the femoral vessels deliberately, insert as large a catheter as possible, place it carefully in position, and thus get a really good angiogram. That was less traumatic than percutaneous techniques, although they were quite successful in adults.

Giant Hæmangioma with Thrombocytopenia.

T. Y. NELSON (Sydney) read a paper entitled "Giant Hæmangioma with Thrombocytopenia" (see page 815).

I. C. LEWIS (Perth) said that Dr. Wallman had recently shown an example of that syndrome in Perth. His patient had presented at the age of three months with one forearm about three times the size of the other. Thrombocytopenia had been present, and there had been much discussion about treatment, several surgeons recommending amputation. However, conservative treatment had been decided on, and two years later the arm was found to have returned to normal size and there was no longer any thrombocytopenia. There was some thickening of the subcutaneous tissue, but very little skin discoloration. Dr. Lewis thought that one had to be very selective in recommending surgery in those cases.

R. SOUTHBY (Melbourne) asked whether there was any indication of an arterio-venous connexion in those cases.

Mr. Nelson replied that no such communications had been demonstrated.

N. NEWMAN (Hobart) said that Dr. J. P. Millar had had a similar case involving the whole forearm, in which the abnormality had subsequently disappeared. However, that case differed from Mr. Nelson's, in that the lesion seemed very superficial and the overlying skin much thinner, and also in that large blood vessels were present coursing superficially in the arm. Mr. Newman asked whether Mr. Nelson differentiated between those two varieties of the condition.

Mr. Nelson replied that it had been suggested that some of those tumours were composed of capillary tissue and others of more cavernous tissue, the former being more liable to regress spontaneously and to respond to X-ray therapy. He did not know whether that could be regarded as a means of distinguishing between those lesions which would subside and those which would not. He himself would not rely on it, because in the lesion he had demonstrated the tissue was mainly capillary; but there were also large cavernous spaces in it.

J. H. COLEBATCH (Melbourne) said that he had come across five cases which could be put into the same category as Mr. Nelson's. The patients had been seen in the neonatal period, and three of them did not have any serious hæmorrhagic disorder. Minimal thrombocytopenia was present, but they were not subject to serious hæmorrhage. One patient in whom serious hæmorrhage had occurred seemed likely to die on the second day of life, both from anæmia and hæmorrhage and from cardiac failure. Not only thrombocytopenia, but also hypoprothrombinæmia and fibrinolysins were present. Although there had been extreme danger from hæmorrhage, the condition had responded to conservative measures. In fact, only one of his patients had not responded to conservative measures. That child had had a serious hæmorrhagic disorder by the end of the

first week, which had progressed so far by the end of the first month that surgery and X-ray treatment had been undertaken, the surgery consisting solely of incision of the tumour to relieve tension. Dr. Colebatch thought that radiotherapy combined with long-term full-dosage steroid therapy might sometimes be an alternative to surgery.

Mr. Nelson said that the point he wished to emphasize was that those tumours should be removed before thrombocytopenia occurred. Commonly they were quite innocuous when first seen, and although many of them regressed without developing any hæmorrhagic tendencies, the case he had quoted showed the danger of waiting. It was not safe to leave those tumours alone, as there was not sufficient evidence to differentiate those tumours which would regress from those cases in which thrombocytopenia would develop.

REPORT OF A SUBCOMMITTEE OF THE AUSTRALIAN PÆDIATRIC ASSOCIATION ON CHILDREN IN HOSPITAL AND PÆDIATRIC EDUCATION.

THE following is the report of a subcommittee appointed by the Executive of the Australian Pædiatric Association on October 9, 1959. The report was adopted by the Australian Pædiatric Association at the Annual General Meeting on April 23, 1960.

The subcommittee consisted of Professor V. L. Collins, Professor L. F. Dods and Professor W. B. Macdonald (Convener).

Terms of Reference.

The terms of reference were to determine for Australian requirements: (i) The relation of a children's hospital or a children's unit to a general hospital with reference to the special needs of children and how they can best be provided in (*a*) a University centre, (*b*) a provincial city or large town, (*c*) a small town, (*d*) the country where the population is scattered. (ii) The part to be played by pædiatric teaching in a medical curriculum.

Purpose of Report.

The purpose of the report is to clarify the attitude of the Australian Pædiatric Association to two important questions affecting the total welfare of children, in view of possible decisions of hospital and university authorities which might affect this welfare.

State representatives were asked to furnish their opinions. These provided good evidence that both matters were worthy of consideration by the Australian Pædiatric Association for the purpose of formulating an official policy.

1. The Relation of a Children's Hospital or a Children's Unit to a General Hospital with Reference to the Special Needs of Children and how they can Best be Provided.

This matter has been considered in detail by numerous committees and individuals, the most authoritative of which are: the Central Health Services Council, Ministry of Health, 1959 (The Platt Committee), and the Pædiatric Committee of the Royal College of Physicians of London, 1957. A list of references is appended. It is unnecessary to reiterate in detail the total substance of some very comprehensive reports, but certain extracts have been quoted as a basis for formulating an official policy of the Australian Pædiatric Association.

In its Summary of Recommendations the Platt Committee states:

> Greater attention needs to be paid to the emotional and mental needs of the child in hospital against the background of changes in attitudes towards children, in the hospital's place in the community, and in medical and surgical practice.

Additional recommendations related to the terms of reference are:

> Children and adolescents should not be nursed in adult wards.
>
> Children should be nursed in company with other children of the same age group. They should have facilities for inside and outside play.
>
> A children's physician should have a general concern with the care of all children in hospital.
>
> The sister in charge of the ward should be R.S.C.N. as well as S.R.N. The child should be able to get to know his own nurse.
>
> The provision of education facilities is important for shorter stay as well as long stay patients.

Extracts from the Report of the Pædiatric Committee of the Royal College of Physicians further support this attitude. The Committee states in its General Considerations:

> The proper care of children in hospital is so different from that of adults that their admission to adult wards is to be deprecated. It is realized that such admissions may sometimes be necessary to obtain investigation and treatment in specialized units, but when this occurs there is a particular need for close liaison with the pædiatric services.
>
> There is no doubt that special children's hospitals offer the best service for children, because the staff, at all levels and in all departments, is attuned to the special needs of the sick child. Children s hospitals carry with them a tradition of service which cannot lightly be set aside.
>
> In large general hospitals a separate self-contained children's block in close association with the obstetric department of the general hospital is desirable. Where there is no separate children's block all children should be in special wards in a single unit under the general supervision of a pædiatrician, with a sister in charge who has had training and experience in nursing sick children. A children's unit makes possible such amenities as schooling and facilities for play, etc. It is most desirable, as suggested by the Ministry of Health, that the consultant pædiatricians of outlying units should, where possible, be connected with central units so that they do not work in isolation.

These recommendations and others by these two authoritative committees are well supported by the attitude of the State representatives of the Australian Pædiatric Association. The unanimous opinion of the Queensland members of the Australian Pædiatric Association exemplifies the general attitude, and is as follows:

> 1. Wherever possible, children should be cared for in a children's hospital where the staff is not interchangeable with that of an adult hospital, for only in this way can the patients be under the care of a staff which—at all levels—properly understands, and is in sympathy with, their special needs. Ideally this should apply to the student nurses as well as the rest of the staff. Nurses graduating from a children's hospital could get an endorsement for adult nursing by an additional short period of training in an adult hospital.
>
> As far as possible the administration of such a children's hospital should be divorced from that of any other hospital.
>
> 2. Where the density of population does not warrant a separate children's hospital, children should be cared for—both as in-patients and out-patients—in a separate wing of an adult hospital remote from adult patients and should have, as far as possible, a permanent staff caring for them. This opinion would also hold in principle, in the case of those children who for special reasons have of necessity to be admitted to an adult hospital for investigation and/or surgical treatment.
>
> 3. Children should on no account be admitted routinely to adult wards on the excuse that this allows both adults and children requiring some specialized medical or surgical care to be congregated together for geographical convenience.
>
> 4. There is something to be said for a children's hospital being in reasonably close proximity to an adult hospital, provided this proximity does not interfere with the autonomy of the children's hospital.

These opinions themselves are supported by conclusions of the Nuffield Foundation Investigation into the Functions and Design of Hospitals, 1958, as expressed by Mr. L. Farrer-Brown, Director of The Nuffield Foundation:

> The Nuffield team is working on the assumption that in future a Children's Department (used not only by the pædiatricians but by all the specialists admitting children) will form an integral part of each major hospital group. The team feels, however, that the arrangement of space and general atmosphere appropriate to children cannot economically and conveniently be fitted into the general design of a block occupied also by adults. They would like to see the

children housed in a small one- or two-storey building of their own within the curtilage of an acute general hospital.

With the background of these opinions the subcommittee considered that when the child population has sufficient density, the best interests of children will be served by providing a separate children's hospital. It cannot be emphasized too strongly that the special children's hospital offers the best service for children because staff at all levels and in all departments is attuned to the special needs of the sick child. Even a special children's hospital needs to be of a certain size before a proper hierarchy of well-trained medical staff—resident medical officers, registrars, pædiatricians—is readily available 24 hours a day, seven days a week, to understand and treat the rapid changes which may occur in the condition of a sick child.

Accordingly it is suggested that the following principles should be adopted by the Australian Pædiatric Association:

1. Major centres of population, including all centres with university medical schools, should have separate children's hospitals with their own nursing staff and ancillary units serving the peculiar needs of children, under separate administration but preferably within the curtilage of an acute general hospital.

2. In a provincial city or large town whose population density does not warrant the provision of a separate children's hospital, a children's block containing one or two children's wards should be provided. These wards would be administered by the medical and lay administration of the hospital, but the senior medical staff should be recognized children's physicians, and ward sisters should be trained in children's hospitals.

Special provision should be made for investigating children in the pathology and radiology departments, whilst educational facilities and occupational therapy should be available. Although visiting physicians and surgeons dealing mainly with adults would have patients in the children's wards, the policy in the management of the wards should be made by a recognized pædiatrician.

Where the child population is sufficiently dense, there should be no justification for this alternative, as a children's hospital can provide so much more. The minimum number of children to justify a separate children's hospital would appear to be approximately 200,000 total population.

3. In a small town, special medical, nursing, and ancillary services for children would be impracticable, and it is anticipated that children who require special investigations or treatment would, in some cases, be transferred to bigger centres. It is suggested, however, that a general hospital in a small country town should be provided with a small children's ward where children could be nursed separately. This would also permit more liberal visiting. Preferably, the nursing sister in charge should have undergone training in children's nursing.

4. In country areas where the population is scattered, the sick would be served by small bush nursing hospitals. If the intake of child patients was not sufficient to justify a children's ward, every attempt should be made to cater for the special needs of small children as closely as possible by adhering to the general principles defined previously and contained in the reports to which reference has been given, especially the Report of the Central Health Services Council, Ministry of Health, 1959 (The Platt Committee).

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2. The Part to be Played by Pædiatric Teaching in a Medical Curriculum.

As with the previous item, this has received particular attention of recent years, and has been covered in a comprehensive and excellent manner by a Study Group on Pædiatric Education working under the ægis of the World Health Organization, Stockholm, 1956. This report has been published as W.H.O. Technical Report No. 119 and should be read by all those who are interested in this subject.

The report deals with undergraduate and post-graduate pædiatric education, and the relationship with other disciplines in the medical curriculum.

It is considered that in view of the fact that opinions have been expressed in Australia that the teaching of pædiatrics can be left to physicians accustomed to dealing with adults, and that pædiatrics can be considered along with other minor specialties, the Australian Pædiatric Association should declare itself in support of the opinions expressed by the W.H.O. Study Group, so that the study of the child in health and sickness can be placed in true perspective in the medical curricula of Australian medical schools.

It is impossible to cover all the facets of this subject but a few pertinent extracts from the W.H.O. Report may be quoted:

Objectives and Role of Pædiatrics in Medical Education.

Medical education has as a basic objective the preparation of good general physicians able to serve the community as well as the individual. Prerequisites in the preparation of such physicians are: (1) the awakening of student interest in the human being, the family and the community; (2) the development of sound habits of study and the continuous desire for self-education; (3) the stimulation of scientific curiosity; and (4) the acquisition of a specific body of knowledge and skills. The competent practitioner must recognize and be responsive to the social needs and health demands of the community and country in which he lives.

Pædiatrics occupies a unique position in the attainment of these objectives. Some of the reasons for ascribing special status to pædiatrics in medical education are:

(a) The care of children comprises a large part of general medical practice. Information from certain countries indicates that child care accounts for at least one-third of total practice and in some countries the proportion is even greater.

(b) There is high morbidity and mortality during early infancy. In large areas of the world sickness and death among infants and children constitute a major public health problem.

(c) Pædiatrics is not a specialty limited to an organ system, to a technique, or to a disease or group of diseases. It is general medicine applied to a specific period of life.

(d) The child, nevertheless, is not a miniature adult. Childhood represents, in the life-time of every human being, the biological period characterized by the process of growth and development which continues from birth through adolescence.

(e) Problems and diseases occur in this age period which do not exist in adult life.

(f) The seeds of many diseases seen in adults, such as rheumatic fever, tuberculosis and the neuroses, are sown in childhood.

Furthermore, pædiatrics provides unequalled opportunities to contribute to the basic objectives of medical education since the factors of growth and development set the stage of meaningful study of the natural history of disease in a constantly changing organism. Childhood is a period in which promotion of health can be carried out effectively by the physician as he supervises the child's progress. The dependent position of the child in the family provides an excellent opportunity for acquainting the student with social and environmental factors which influence human well-being. In dealing with parents and children, the student must be

taught to exercise perspicacity, patience and gentleness, qualities which are desirable throughout the practice of medicine.

The Group considered it essential that pædiatrics constitute one of the major subjects of the medical curriculum.

The Group agreed that it was impossible to do justice to the pædiatric curriculum with fewer than 300 hours as a minimum. The allocation of one quarter of the clinical time to pædiatrics was envisaged as a reasonable proportion.

Instruction in pædiatrics should not be limited to any one year but should extend throughout the curriculum, independently and in collaboration with other departments, both pre-clinical and clinical, and there should be a concentrated period of pædiatric training towards the end of the medical studies.

Much of the report is confined to teaching methods which are not germane to the issue presented to the Australian Pædiatric Association. The main purpose of this presentation is to obtain the support of members in an endeavour to encourage, by concerted action, the implementation of the principles set down by the W.H.O. Study Group, in view of powerful influences which may attempt to impose teaching policies contrary to these principles and the ultimate welfare of children in Australia.

It is suggested that the Australian Pædiatric Association make the following recommendations in relation to the part to be played by pædiatric teaching in a medical curriculum:

1. Pædiatrics should constitute one of the major subjects of the medical curriculum and should not be regarded as a minor specialty.

2. Instruction in pædiatrics should not be limited to one year but should extend throughout the curriculum, independently and in collaboration with other departments, both preclinical and clinical.

3. At least 300 hours should be given to the study of pædiatrics.

4. Every medical school should have its chair of child health, with a professorial unit established in the main children's teaching hospital.

5. There should be a close working relationship between the university department of child health, the children's hospital, and the child health services in the community. The university department of child health should have access to all branches of the community health services and social agencies providing care for children.

6. Instruction in child health and disease should be given by or under the direction of physicians and surgeons with special training in children's work, that is, recognized pædiatricians working full time with children. Instruction in diseases of children should be given in children's hospitals with full out-patient facilities and ancillary services so as to present the study of sick children in true perspective. This is not possible where students are taught in a children's ward attached to a general hospital.

7. Examinations in subjects dealing with children in health and disease should be held throughout the medical curriculum, as well as constituting a considerable proportion of the written and clinical examinations for final M.B., B.S.

8. Every endeavour should be made to project these principles into post-graduate education, not only in preparation for specialist training in children's diseases, but in the wider fields of medicine, surgery, and obstetrics.

British Medical Association.

ANNUAL MEETING, AUCKLAND, 1961.

As previously announced, the 129th Annual Meeting of the British Medical Association will be held on February 6 to 10, 1961, at Auckland, New Zealand. The following details relating to the meeting are published at the request of Dr. Anthony T. Hunter, Honorary Joint Secretary.

Office Bearers of Sections.

Section of Anæsthesia.—President, Dr. W. D. Wylie (London); Vice-Presidents, Dr. L. Travers (Melbourne), Dr. G. F. V. Anson (Auckland); Honorary Secretary, Dr. W. J. Watt (Auckland).

Section of Dermatology.—President, Dr. H. J. Wallace (London); Vice-Presidents, Dr. I. B. Sneddon (Sheffield), Dr. Russell Thomas (Auckland); Honorary Secretary, Dr. P. B. Fox (Auckland).

Section of General Practice.—President, Dr. J. H. Hunt (London); Vice-Presidents, Dr. Mary Esselmont (Aberdeen), Dr. C. L. E. L. Sheppard (Christchurch); Honorary Secretary, Dr. T. D. C. Childs (Auckland).

Section of Medicine.—President, Professor Sheila Sherlock (London); Vice-Presidents, Professor T. Russell C. Fraser (London), Dr. W. E. Henley (Auckland), Honorary Secretary, Dr. D. Hanna (Auckland).

Section of Neurology and Neurosurgery.—President, Mr. J. E. A. O'Connell (London); Vice-Presidents, Mr. D. D. McKenzie (Auckland), Dr. I. M. Allen (Wellington); Honorary Secretary, Mr. P. Wrightson (Auckland).

Section of Obstetrics and Gynæcology.—President, Professor T. N. MacGregor (Edinburgh); Vice-Presidents, Professor Gordon King (Perth), Mr. L. C. L. Averill (Christchurch); Honorary Secretary, Mr. I. B. Faris (Auckland).

Section of Ophthalmology.—President, Mr. Frank Law (London); Vice-President, M. Howard Coverdale (Auckland); Honorary Secretary, Mr. C. C. Ring (Auckland).

Section of Orthopædic Surgery.—President, Mr. H. Jackson Burrows (London); Vice-Presidents, Mr. J. S. Batchelor (London), Mr. J. K. Elliott (Wellington); Honorary Secretary, Mr. Harman Smith (Auckland).

Section of Oto-Rhino-Laryngology.—President, Mr. Myles L. Formby (London); Vice-Presidents, Mr. J. Angell-James (Bristol), Mr. E. I. A. MacDonald (Auckland); Honorary Secretary, Mr. C. B. Cornish (Auckland).

Section of Pædiatrics.—President, Professor W. Gaisford (Manchester); Vice-Presidents, Professor L. Dods (Sydney), Dr. S. L. Ludbrook (Auckland); Honorary Secretary, Dr. A. M. Bush (Auckland).

Section of Pathology.—President, Dr. C. J. C. Britton (London); Vice-Presidents, Dr. R. J. Walsh (Sydney), Dr. J. O. Mercer (Wellington); Honorary Secretary, Dr. S. E. Williams (Auckland).

Section of Psychiatry.—President, Dr. Desmond Curran (London); Vice-Presidents, Professor W. H. Trethowen (Sydney), Dr. Doris M. Odlum (Bournemouth); Honorary Secretary, Dr. H. R. Bennett (Auckland).

Section of Radiology.—President, Professor B. W. Windeyer (London); Vice-Presidents, Dr. Thomas Lodge (Sheffield), Dr. D. Urquhart (Palmerston North), Dr. A. C. Begg (Dunedin); Honorary Secretary, Dr. T. Thomas (Auckland).

Section of Rheumatology.—President, Dr. W. S. Tegner (London); Vice-Presidents, Dr. M. Kelly (Melbourne), Dr. A. Rowatt Brown (Auckland); Honorary Secretary, Dr. F. Swan (Auckland).

Section of Surgery.—President, Sir Arthur Porritt (London); Vice-Presidents, Mr. A. Dickson Wright (London), Professor P. J. Moir (Leeds), Professor J. Loewenthal (Sydney), Professor G. J. Fraenkel (Dunedin); Honorary Secretaries, Mr. Warwick Macky (Auckland), Mr. D. B. Rogers (Auckland), Mr. B. Barratt-Boyes (Auckland).

Outline of Events.

The scientific programme extends from Monday, February 6, to Friday, February 10, but during the preceding week-end there will be time allotted for registration and certain social activities. The following is an outline of events.

Friday, February 3: Registration, commences 9 a.m. to 4 p.m.; visit to Kinleith, the timber, board and paper mills of New Zealand Forest Products near Tokoroa.

Saturday, February 4: Registration, 9 a.m. to 4 p.m.; service at the Synagogue; sport and social activities.

Sunday, February 5: 9 a.m., Holy Mass at St. Patrick's Cathedral; 11 a.m., Anglican service; 3 p.m., garden party at the home of Sir Frank and Lady Mappin; 8 p.m., theatre—film premiere at the Odeon Theatre.

Monday, February 6: 9 a.m., Council Meeting of the New Zealand Branch of the British Medical Association; 9 a.m., opening of Trades Exhibition by Sir Douglas Robb; 11 a.m., opening of conference by His Excellency the Governor-General; 11.30 a.m., inaugural address, Professor E. Sayers, Dean of Otago University Medical School; induction of the President of the New Zealand Branch of the British Medical Association; 2.30 p.m. to 4 p.m., plenary session ("Maintain-

ing the Health of the Middle-Aged Executive"); 8 p.m., annual general meeting of the British Medical Association, presidential induction, address and reception.

Tuesday, February 7: 8 a.m., Christian Medical Fellowship breakfast; 9 a.m., Council Meeting of the New Zealand Branch of the British Medical Association; 10 a.m., day visit to Wenderholme beach and Waiwera Hot Springs; 9.30 a.m. to 11 a.m., plenary session ("The General Surgical, Medical and Psychological Problems of Pregnancy"); 11.30 a.m. to 12.30 p.m., round table conference ("The Present Position of Steroid Therapy"), and sectional meetings; 2.15 p.m. to 4.30 p.m., sectional meetings; 7.30 p.m., conference dinner at the Australian Pavilion, Epsom Showgrounds.

Wednesday, February 8: 9.30 a.m. to 11 a.m., plenary session ("Chemotherapy in Cancer"); 11.30 a.m., launch trip on Waitemata Harbour.

Thursday, February 9: 9.30 a.m. to 11 a.m., plenary session ("Iso-Immunization—A New Concept of Disease"); 11.30 a.m. to 12.30 p.m., round table conference ("Ulcerative Colitis") and sectional meetings; 2.15 p.m. to 3.15 p.m., sectional meetings; 4.30 p.m., afternoon reception by the B.M.A. at Ellerslie Racecourse.

Friday, February 10: 9.30 a.m., visit to Puketutu Island on Manukau Harbour; 9.30 a.m. to 11 a.m., plenary session ("Mental Health in the Community"); 11.30 a.m. to 12.30 p.m., round table conference ("Thyroid Disease") and sectional meetings; 2.15 p.m. to 3.15 p.m., sectional meetings; 3.45 p.m., annual general meeting of the New Zealand Branch of the British Medical Association; 4.45 p.m., War Memorial Oration at the Auckland Grammar School—speaker, Mr. Kenneth MacCormick, C.B., C.B.E., D.S.O., F.R.C.S., F.R.A.C.S.; 9 p.m., Conference Ball in the Town Hall.

Plenary Sessions.

Monday, February 6, 2.30 p.m. to 4 p.m., Town Hall, "Maintaining the Health of the Middle-Aged Executive": chairman, Dr. D. Rogers (Hamilton); speakers, Dr. J. H. Hunt (London), Dr. J. J. O'Dwyer (London), Dr. Muriel Bell (Dunedin), Dr. G. P. Hallwright (Wellington); official reporter, Dr. D. Hanna (Auckland).

Tuesday, February 7, 9.30 a.m. to 11 a.m., Town Hall, "The General Surgical, Medical and Psychological Problems of Pregnancy": chairman, Mr. A. Macfarlane (Auckland); speakers, Professor T. MacGregor (Edinburgh), Mr. A. Dickson Wright (London), Dr. Desmond Curran (London), Mr. J. S. Batchelor (London); official reporter, Mr. I. B. Faris (Auckland).

Wednesday, February 8, 9.30 a.m. to 11 a.m., Town Hall, "Chemotherapy in Cancer": chairman, Professor E. G. Sayers (Dunedin); speakers, Professor F. Bergel (London), Dr. A. Freedman (Sydney), Mr. A. Lawrence Abel (London); official reporter, Mr. D. B. Rogers (Auckland).

Thursday, February 9, 9.30 a.m. to 11 a.m., Town Hall, "Iso-Immunization—A New Concept of Disease": chairman, Sir Charles E. Hercus (Dunedin); speakers, Dr. R. J. Walsh (Sydney), Dr. I. M. Roitt (London), Dr. J. O. Mercer (Wellington); official reporter, Dr. A. M. Bush (Auckland).

Friday, February 10, 9.30 a.m. to 11 a.m., Town Hall, "Mental Health in the Community": chairman, Dr. G. Blake-Palmer (Wellington); speakers, Dr. D. W. Johnson (Brisbane), Dr. Doris Odlum (Bournemouth), Professor W. Trethowan (Sydney), Dr. V. McGeorge (Auckland); official reporter, Dr. H. Bennett (Auckland).

Round Table Conferences.

Tuesday, February 7, 11.30 a.m. to 12.30 p.m., Town Hall, "The Present Position of Steroid Therapy": chairman, Dr. W. E. Henley (Auckland); panel, Professor Sheila Sherlock (London), Dr. W. D. Wylie (London), Dr. W. S. Tegner (London), Dr. H. J. Wallace (London), official reporter, Dr. J. D. K. North (Auckland).

Thursday, February 9, 11.30 a.m. to 12.30 p.m., Town Hall, "Ulcerative Colitis": chairman, Dr. J. W. Bartrum (Paeroa); panel, Mr. G. E. Moloney (Oxford), Mr. A. Lawrence Abel (London), Mr. Harold Dodd (London), Dr. A. P. Millar (Sydney); official reporter, Mr. W. I. Cawkwell (Auckland).

Friday, February 10, 11.30 a.m. to 12.30 p.m., University, "Thyroid Disease": chairman, Mr. K. McNamara (Auckland); panel, Professor T. Russell C. Fraser (London), Professor G. T. Fraenkel (Dunedin), Professor B. W. Windeyer (London), Dr. B. Hamilton (Hobart); official reporter, Dr. H. K. Ibberston (Auckland).

Out of the Past.

WET NURSING.

[From "What Kills Our Babies", by Charles D. Hunter (Australian Health Society, Melbourne, 1878). The pamphlet contains much practical advice, and is an interesting reflection of current social conditions and pædiatric practice.]

MANY a mother who thoughtlessly gives up nursing her own child little knows the risk to which she puts it. A wet-nurse can never be as safe as a mother. Babies cannot live by milk alone, and petting, and joy in her child go far to carry it safe through the dangers of the first year. Thus a clever French doctor who studied this matter gives it as a fact that while out of a hundred children suckled by their own mothers about eighteen died in their first year, twenty-nine died who were suckled by wet-nurses. Let no mother then lightly refuse her motherly duties. Nursing is good for both her and the child . . . . Let mothers remember this, as well as the fact that at least one baby out of every eight is killed by the change from the mother's breast to the wet-nurse's. I well remember how earnestly our professor of medicine in the university at home warned us never to countenance the use of a wet-nurse except for some very good reason. He is still alive, a celebrated doctor, and one of Her Majesty's physicians. Besides the risk to the child itself, there is the more terrible risk to the wet-nurse's child—a risk four to one if it is to be brought up entirely by hand. Dare any mother, then, for mere ease, convenience, or fashion, sacrifice the life of her nurse's child? "The doctor allowed me" is no excuse, unless real and dangerous illness were present. It has been seen that about eighteen children die in the hundred when nursed by their mothers, but eighty in the hundred die under hand-feeding—four times as many, and this too in a carefully-conducted home under medical supervision; but what must it be when the wet-nurse's child is handed over to some ignorant old woman? At the best we see out of every five babies brought up by hand four die in their first year. But it may be confidently stated that farmed-out as a poor wet-nurse's baby is likely to be in Melbourne, many more will die, and the fashionable mother who employs a wet-nurse may be certain that in six cases out of seven she has killed the wet-nurse's child. Will the doctor share this responsibility with her? The figures are from the recognized text-books on the subject; every doctor can easily find them if he wants to.

But the wealthy are not alone to blame in this matter. I have seen more children by far brought up by hand because the mother went out to work than for any other reason; and, worse still, often simply because the father was too idle, too proud, or too drunken to work. I fear it is idle pleading with such men for the lives of their children. We have in Melbourne hundreds of men who, because they have once been clerks or drapers, will not, they say, "stoop" to do "manual labour". Yet they can stoop to live on their wife's earnings, and to kill their children.

Special Correspondence.

LONDON LETTER.

FROM OUR SPECIAL CORRESPONDENT.

The National Health Service.

IN a foreword to the annual report of the Ministry of Health for 1959, the Minister, Mr. Derek Walker-Smith, Q.C., M.P., looks forward to continued and more rapid progress, particularly in the hospital building programme. Work has started on nine new hospitals, eight are partly complete and a further 17 are in the planning stage. The Minister describes as the most important single event during 1959 the passing into law of the *Mental Health Act*, a notable achievement in social progress. This Act provides a completely new legal framework for the admission of the mentally ill patient to hospital, and completes the integration of all the services concerned with health into the National Health Service. In future, general hospitals may be expected to provide for the screening of all types of mental illness and include out-patient treatment.

The Cost of the Service.

The report shows that the total cost of the health service for 1959 was £671 million (£45 million more than the previous year). The amount borne by the Exchequer was £486 million —i.e., three-quarters of the total; the remainder comes from National Health Service contributions, charges to persons using the service (payments to dentists and opticians and for drugs supplied), superannuation contributions, and Local Authority rates. The cost of the various divisions of the service:

Hospital services	£383 million.
General medical services	£66 million.
Pharmaceutical services	£69 million.
Dental service	£46 million.
Local Authority services	£59 million.

All showed an increase over the previous year.

Staffing the Hospitals.

Every year since the inception of the service, the total number of consultants has increased, and by the end of 1959 had reached 7102. The numbers in all categories of nursing staff increased significantly during the year. There was an improvement in the hospital midwifery strength, but the shortage is still acute in some areas.

General Practice.

Two major trends have developed in the health service in recent years: (i) the emphasis on preventing illnesses and (ii) the policy of providing more medical care in the home rather than in the hospital. The trend towards group partnerships has continued, and there are fewer single-handed practitioners. The average number of names on a doctor's list over the country as a whole in July, 1959, was 2282, and the average net remuneration £2426 *per annum*.

Future of the Tuberculosis Service.

The dramatic decline in the incidence of tuberculosis in all but the oldest age groups during the past 10 years provides an opportunity for considering the future of this old-established service with its specialist physicians, chest clinics and sanatoria. The Minister of Health has commended the recommendations of the Standing Tuberculosis Advisory Committee for the gradual integration of the tuberculosis service into the general hospital service. The normal pattern of the future is that appointments in chest diseases should be to the staffs of general hospitals, the chest clinic forming part of the general out-patient department and sharing the general services of that department. Existing sanatoria and chest hospitals would be used as departments of nearby general hospitals or be run in close association with them. In new hospitals, beds would be provided for diseases of the chest, some being set aside for tuberculosis. The chest physician must continue to work closely with the medical officer of health on the epidemiological and preventive aspects of tuberculosis, in order to attain the end of its epidemic prevalence in the community.

Maternal Mortality.

A report on the Confidential Inquiry into Maternal Deaths was first published in 1957. A further report, a continuation of this inquiry covering the years 1955 to 1957, is now available. Over the period under review, over two million births took place without fatality, but 1480 maternal deaths were reported, and this forms the subject of the latest report. Since the previous report, there has been a general reduction of about one-fifth in the number of maternal deaths. The four main causes are: toxæmia (22%); pulmonary embolism (17%); abortion (16%); hæmorrhage (14%). Deaths from toxæmia have been reduced by one-fifth and from hæmorrhage by about one-third since the last report.

The risk of death in childbirth might have been lessened by avoidable factors. Excluding deaths due to abortion, in some cases the patient herself was wholly or partially responsible; but avoidable factors were also present in hospital cases and in the domiciliary service. Mistakes in the domiciliary service cannot be attributed to the hospital service or vice versa, and it is not possible to compare the two services. It is hoped, by publishing this report, to enable those concerned with the care of the expectant and parturient mother to identify the main avoidable factors and to anticipate them by appropriate action.

Premature Births.

At the present time, prematurity accounts for over 5500 registered infant deaths in England and Wales. The prevention of premature births and the care of the premature infant are the subject of a report from a subcommittee of the Central Health Services Council. The report briefly reviews the causes of prematurity, as far as they are known, and the factors influencing survival. Measures suggested to reduce mortality include the establishment of specialized centres in the larger maternity departments catering for abnormal obstetrics in each hospital area, where all women who go into labour before the twenty-seventh week of pregnancy could be admitted, and where special baby-care units would be provided. The optimum size of the unit would not be less than 20 cots, adequate to serve a population of 200,000. For the premature infant born at home and removed to a special unit, better transport facilities and the establishment of an emergency resuscitation unit team would help to reduce mortality.

More research on the factors causing premature labour is urgently needed.

Congenital Abnormalities.

Experts from many countries met in London in July for the first International Conference on Congenital Malformations, each contributing his specialized knowledge in an attempt to elucidate the genetic and environmental factors involved in congenital malformations. The virologist studying the effect of maternal rubella, the physicists studying the hazards of radiation, the geneticists studying chromosomal abnormalities in mongolism, by meeting with other specialists may find some common links with the causation of these malformations.

A recently published report on the hazard of rubella and other virus infections during pregnancy is the result of a survey made over the years 1950 to 1957. The investigation was undertaken because of the report from Australia in the early 1940's, which suggested that congenital malformations occurred in "seriously high frequency" when rubella occurs in pregnancy. Although later reports suggested that the risk was not as great as at first feared, it was not known just what was the chance of a mother who had rubella having a deformed child, compared with that of a mother who did not have rubella. From the report, it is confirmed that the health hazard to babies whose mothers have rubella is not as great as was once feared. Altogether, 7396 expectant mothers, 1679 of whom had a virus infection and 5717 who had no such infection, were studied. Their babies were periodically examined up to two years of age. There were 578 pregnancies complicated by rubella, which produced 547 live children, of whom 37 had major congenital defects. In the control series of 5717 pregnancies there were 5469 live-born children, of whom 128 had major defects. The main differences between the rubella and the control series were that, in pregnancies in which rubella occurred during the first twelve weeks, there was a higher proportion of abortions and stillbirths, a higher proportion of babies who failed to survive to their second birthday, a higher proportion of babies with congenital malformations, particularly those of the heart, eye and ear, and a higher proportion of babies of low birth weight.

Just under 16% of these rubella babies had abnormalities, compared with 2% to 3% of control babies.

Most of the children of mothers who had rubella in early pregnancy, were examined again at ages from two to five years, when several cases of previously undetected impairment of hearing were found. No new defects were brought to light.

It is considered that the occurrence of deafness should be especially looked for in all children born to rubella mothers. Impairment of hearing following rubella within the first 12 weeks of pregnancy is about 19%. In only a small number of affected children was deafness a severe handicap, two-thirds of them being able to attend an ordinary school.

The effects of other virus infections—measles, chicken-pox, mumps, poliomyelitis and influenza—were also studied, but it was found that these did not have the same deleterious effect as did rubella in the first three months of pregnancy.

Handicapped Children.

"In recent years, our attitude to seriously handicapped children has greatly changed." Sir John Charles, Chief Medical Officer of the Ministry of Health, makes this statement in the preface to a report on the development of children by Dr. Mary Sheridan. The report, the result of an extensive study of development in early childhood, is in two parts. The first emphasizes that the younger the age at which children with physical, mental or emotional disabilities are discovered and assessed, the more hopeful

is the prognosis for recovery or habilitation. Case-finding depends upon the recognition of the earliest signs of deviation from normal development; hence it is essential that all medical practitioners who deal with children should be familiar with the accepted "stepping stones' of development. The second section consists of a description, in chart form, of the behaviour of young children at significant ages up to five years, and includes the tests employed to assess the degree of development attained. These tests relate to posture and large movements, vision and fine movements, hearing and speech, social behaviour and play.

Correspondence.

AN AUSTRALIAN MEDICAL ASSOCIATION.

SIR: We, the undersigned, having given careful consideration to the draft constitution of the Australian Medical Association, would make the following observations:

1. No person should have double representation. Accordingly, the constitution should be altered to eliminate voting representation of the affiliated organizations (Colleges, etc.). Their representatives can be invited to meetings when their special interests (as a body) are affected. Members of these special groups should join their local association and be represented through it.

2. The constitution of Federal Council should be in proportion to the numerical strength of each constituent association (State bodies)—say, one representative for the first 250, plus one representative for each additional 1000 members. Also, election to the council of each constituent association should be on a regional basis, thus ensuring representation of all sections of medical opinion.

Those elected as representatives should reflect medicine as a whole, and not any special group.

Yours, etc.,
K. WHITE,
J. MULLER,
H. ROSE,
R. DAN,
J. SULLIVAN.

17 Bolton Street,
Newcastle,
New South Wales.
November 1, 1960.

DEVELOPMENTS IN OUTBACK MEDICAL SERVICES.

SIR: I would like to congratulate you on your leading article on the Royal Flying Doctor Service published on October 15, and entitled "Developments in Outback Medical Services".

Your appeal is to "Development". This appeal applies respectively to each State, and more particularly to New South Wales. The organization in each State is (unfortunately in some ways) quite separate and independent. Overlapping across State boundaries is inevitable and is all to the good at present. But there could be more cooperation.

Time was, and still is, when the combination of doctor, radio and aeroplane existed for the public in a distant mist of glamour, which served a purpose in attracting romantic interest and charitable help. It is time, however, that this mist was dissipated and the Service recognized for what it is—namely, an essential medical service to a certain somewhat voiceless section of the community. This section is composed of human beings and families no less real because they are out of sight, and no less prone to accident, illness and anxiety.

Whilst there is always a place for charity in all things medical, there is no place for patronage in this case. These people are entitled to the service they have, and their ideas on future development must be taken into consideration. The vast pastoral industry of inland Australia makes the inland family an important factor in the Australian economy. Apart from that consideration is the fact that these people themselves contribute heavily towards the cost of the Royal Flying Doctor Service. This contribution, together with subsidy from the Governments (State and Federal), constitutes in New South Wales at least half the annual costs of the Service.

As stated in your article, "outback people should get the best medical service possible". With this principle in view, one is faced by certain disadvantages in the present administration of the New South Wales section. These disadvantages should be faced. The chief disadvantage is the remoteness of the controlling body in Sydney from the scene of operations around Broken Hill. The impact of medical requirements and the significance of the occasional emergency are lost in transit over seven hundred miles to Secretary, to President and to next monthly meeting. About once a year a tragedy will occur at night. A luckless Australian Inland Mission sister and her more luckless patient were overtaken one night by retained placenta and post-partum hæmorrhage at Birdsville, 450 miles north of Broken Hill and 350 miles west of Charleville, the two nearest bases. Here is a problem indeed. Nearer home, at a homestead 170 miles north of Broken Hill, a child slipped one night in the bath, struck her head and sustained a cerebral hæmorrhage from which she died at 1 a.m. Others could be quoted.

There was a widespread request in 1954 for the development of night rescue. It was discarded by the Sydney Flying Doctor Council on the score of expense and risk. Since then no progress whatever has been made towards the fitting up of even one airstrip in the whole area for a possible night landing. This important matter should be referred to consultation on a wide basis with professional aviation, including the Department of Civil Aviation. Graziers who now fly their own aircraft over the West Darling area should have a voice in the matter.

Only one night flight has been undertaken since 1954, and that would not have been possible had not the Zinc Corporation at Broken Hill supplied their aeroplane and their two pilots for the emergency. The chief pilot of the Royal Flying Doctor Service at Broken Hill decided that the Royal Flying Doctor Service Drover aircraft was unsuitable for the flight. Night flights out from Broken Hill are never undertaken by the aircraft of the Royal Flying Doctor Service.

It is generally realized, of course, that night flying cannot be lightly undertaken; the risks of getting lost are too great. But on the other hand, some start should be made towards equipping at least one airstrip in a strategic position of the back country, with beacons and landing lights and guidance to it from Broken Hill. If successful, other night-landing airstrips would follow. Temporary bases would thus be available in an emergency at night, from where the doctor could proceed further by car. Getting blood rapidly to where it is required is the ideal to aim at. The urge for this line of development arises with each fresh tragedy and then is forgotten again. Only a few weeks ago, a man from Tilpa, 100 miles south-west of Bourke, had an arm torn off at night. He was taken by car to Bourke and died. Hours of travel over bad roads probably sealed his fate.

A different line of development, in which Queensland appears to lead, is the provision of regular clinics at centres throughout the outback. These clinics are of great value to the people, and are every bit as important as the emergency part of the Service. Several more should be opened in the far west of New South Wales; but with only one doctor available, this is hardly possible. Queensland puts the emphasis on the flying doctor, on the medical side of the Service. New South Wales puts the emphasis on the aeroplane ambulance.

The time has come when New South Wales should consider the appointment of a second flying doctor, and even of a third.

In Queensland they have three bases and four doctors. In New South Wales we have only one base and one doctor. In Queensland they have a medical travelling manager, Dr. Vickers (making a fifth doctor in the Queensland Service). In New South Wales there is a lay travelling manager appointed this year.

The base at Broken Hill could be more economically managed with a view to giving a larger medical service. That base is costing around £40,000 a year, more than £100 a day. Flying costs and pilots' salaries account for about half this expenditure. Three radio technicians at the base radio station handle about £25,000 worth of radio telegrams *per annum*. (The radio telegram is the means of communication with the outside world used by outback homesteads.) But of this large figure only about one-fifth comes back to the coffers of the Royal Flying Doctor Service. The rest goes to the post office. Our paid employees to this extent are exploited by the Postmaster-General's Department.

Two pilots are retained at Broken Hill on full award salaries plus bonus payments, and a house and motor-car supplied to the senior pilot. Flying costs and salaries as already stated amount to about ten shillings in the pound at Broken Hill, as against a cost of less than two shillings in the pound for medical salary and expenses.

There is not enough work for two pilots, and therefore the question of chartering a pilot as required, as is done in Queensland, should be considered. If found more economical financially, it could well be adopted, for the system works very well in Queensland, in spite of their greater mileage.

Lastly, the time has come for the establishment of at least one more base in New South Wales. The natural place to select would seem to be Bourke, where there is a first-class airfield, and a big surrounding district hardly touched by the Royal Flying Doctor Service and rarely serviced by either Broken Hill or Charleville bases. A second flying doctor could be based at Bourke with great advantage to the Service, and to the people of a vast circle of country around with a radius of 100 miles. This was the country once served by Nancy Bird and her ambulance aeroplane. Nowadays the sick and injured have to be brought into Bourke by car over bad roads and great distances. This area calls urgently for more service from the Royal Flying Doctor Service. A flying surgeon could be stationed with advantage at Bourke, as the Queensland Service has done at Longreach. Furthermore, from Bourke as a centre, the clinics at Wanaaring and at Hungerford could be more frequent and more economically managed than from the distant base at Broken Hill. The people of the "network", that is to say, the subscribers to the base at Broken Hill, have no opportunity ever to meet together at one time and at one place. Therefore every facility should be given to them to discuss their problems over the air. The "meeting on the air" has, in fact, become quite recently an established method of procedure.

Yours, etc.,

Sydney. C. R. R. HUXTABLE.
October 30, 1960.

PHENYLBUTAZONE VERSUS THE STEROIDS.

SIR: The authors of two recent papers[1,2] recording the abuse of the unique antirheumatic agent phenylbutazone have not tried to differentiate between right and wrong ways of handling it. At the same time they have drawn attention to the disastrous effects of the steroids. Dr. Syme's aged patient with temporal arteritis became œdematous after taking 600 mg. of phenylbutazone daily for an unstated time; then dexamethasone caused muscular wasting. The errors were that phenylbutazone should never be given to aged people, and seldom in doses above 300 mg. daily; it should be withdrawn when undesirable effects appear.[3] In a paper on anæmia after phenylbutazone Dr. Gale and Dr. de Gruchy reported four patients: (i) One continued to take phenylbutazone for two months, then prednisone for three months after developing anæmic symptoms. (ii) Another took 400 mg. for four months and continued for three weeks after appearance of toxic symptoms (fever and sore throat). These were wrongly diagnosed as pharyngitis and treated with penicillin. (iii) A patient of 70 took phenylbutazone for two years before becoming anæmic. (iv) A man of 74 took it without supervision for two years, and continued for six weeks after becoming anæmic. In all four the accepted rules of prescribing phenylbutazone were broken, but the authors did not say so.

It is a pity well-informed doctors should have no opportunity of learning the truth about a drug which has relieved more pain during the past eight years than any other single medical factor. Stranger still is this: younger patients who may safely take phenylbutazone cannot get it under the National Health Scheme, while it is provided free to pensioners, mostly old and endangered by it.

The following undesirable effects in the four cases were not due to the phenylbutazone but to the steroids used for the anæmia: Case 1: ". . . her life was in danger from bleeding *and possibly from infection*". Case 2: *"Two episodes of infection* caused temporary depression of the hæmatological response". Case 3: death from a stroke two days after the daily dose of prednisone had been increased to 60 mg. Case 4: severe infection of throat; fatal stroke. Since 1951 more than 20 authors have seen irreversible brain changes, mostly fatal, from steroids. Recently a dozen articles about "rheumatoid neuropathy" have in fact described irreversible, mostly fatal steroid myelitis. Ten authors have reported convulsions, nine hypertensive encephalopathy (one in Melbourne[4]); there are dozens of reports of psychoses, often suicidal.

I have doubted the prudence of using steroids for blood disorders since I read many reports by hæmatologists of infections and other disasters.[5,6,7] The statistics of the medical Research Council[5] and of D. N. Mohler and B. S. Leavell[8] show no advantage of treated over untreated. And anæmia or purpura developing during steroid treatment of non-fatal diseases has contributed to at least five deaths;[8,9,10,11,12] hundreds of fatal hæmorrhages have occurred without primary blood disorders. Ecchymoses are common effects of all steroids including "Medrol"[7,13] and triamcinolone.[14]

The fashion of ignoring phenylbutazone compels urgent use of steroids for a dozen new but ill-defined diseases which are "absolute" indications. It is stated again and again without proof that the aged patients who get temporal arteritis will go blind if not given tremendous steroid doses. But the strongest evidence quoted by the enthusiasts shows only that the vision of 20 patients with temporal arteritis and defective vision got neither better nor worse after steroids.[15] And temporary[4] or permanent blindness (thrombosis,[6] panophthalmitis,[11] scleromalacia perforans,[16] herpetic ulceration,[17] glaucoma[7]) has often followed steroids.

Rare non-fatal diseases like scleroderma and lupus erythematosus become common and frequently fatal.[4,18] On investigation we find the scleroderma is nearly always an old rheumatoid with a long history of attacks of arthritis of the wrists, and fingers thickened through disuse.[4,18] The lupus cases are mostly indistinguishable from rheumatoid and are diagnosed on L.E. cells alone. But L.E. cells are found in one in four rheumatoid patients.[19,20] The rheumatoid patient gets steroids free under N.H.S. as soon as L.E. cells are found. When he dies we murmur about the high mortality of the collagen diseases—non-existent 10 years ago. Common non-fatal diseases have developed frightening death rates (7 dead out of 29 asthmatics in 30 months;[21] 4 out of 115 with dermatitis in a few months[22]).

It is known since 1950 that the skeletons of the steroid-treated become decalcified. Twenty-six out of 226 patients had 126 fractures; one died through collapse of the chest wall.[23] There has so far been little criticism of the incredible fashion of giving steroids for tuberculosis and acute "cryptogenic" fevers. The compulsion-neurosis which obliges us to use steroids today prohibits discussion of their dangers or thought on the probable plight of the patient in three months.

Yours, etc.,

410 Albert Street, East Melbourne. MICHAEL KELLY.
October 17, 1960.

GENERAL PHARMACEUTICAL BENEFITS.

SIR: The inclusion of any drug in the list of pharmaceutical benefits presumably leads to its increased use by medical practitioners, for not only must physicians be influenced by the cost of drugs to the patient, but also

[1] MED. J. AUST., 1960, 2: 420 (September 10).
[2] MED. J. AUST., 1960, 2: 449.
[3] *Brit. med. J.*, 1959, 1: 1087 (April 25).
[4] *Alfred Hospital Clin. Rep.*, 1959, 9: 33.
[5] *Brit. med. J.*, 1953, 2: 1400 (December 26).
[6] *Pediatrics*, 1957, 19: 95 and 272 (January and February).
[7] *Metabolism*, 1958, 7: 543 (July).
[8] *Ann. intern. Med.*, 1958, 49: 326 (August).
[9] *A.M.A. Arch. Path.*, 1954, 58: 354 (October).
[10] *Brit. med. J.*, 1956, 1: 1075 (May 12).
[11] *N.Y. State J. Med.*, 1958, 58: 3461 (November 1).
[12] *Sem. Hôp. Paris*, 1958, 34: 3179 (December 24); *J. Amer. med. Ass.*, 1959, 169: 1961 (April 18).
[13] *Metabolism*, 1958, 7: 482 (July 1).
[14] *Brit. med. J.*, 1959, 1: 1259 (May 16).
[15] *J. Amer. med. Ass.*, 1957, 163: 821 (March 9).
[16] *Rev. méd. Nancy*, 1959, 84: 735 (July).
[17] *Brit. med. J.*, 1959, 1: 1116 (April 25).
[18] *A.M.A. Arch. intern. Med.*, 1960, 105: 607 (April).
[19] *Ann. rheum. Dis.*, 1955, 14: 415 (December).
[20] MED. J. AUST., 1957, 1: 900 (June 29).
[21] *Lancet*, 1957, 2: 666 (October 5).
[22] *Brit. med. J.*, 1954, 2: 1307 (December 4).
[23] *Canad. med. Ass. J.*, 1960, 83: 376 (August 20).

there will be a tendency to regard the selection of drugs as having been made by an expert committee.

It is particularly unfortunate that, in the case of hypotensive drugs, the choice seems to have been arbitrary and does not follow the current practice in hypotensive clinics in Australia and New Zealand, the United Kingdom or the U.S.A. Of the autonomic blocking drugs listed, "Ansolysen" has been discarded by almost all clinics, because of its capricious absorption; "Darenthin", which has just been added to the list, has the same disadvantage, and in addition the rapid development of tolerance and the marked day-to-day fluctuations in blood pressure make the use of this drug so difficult that we, like others, no longer use it. "Mevasine", which remains in the list, is the only autonomic blocking agent which we would regard as satisfactory, which is listed. However, individual hypertensive patients require individual management, and although in general, "Mevasine" is a satisfactory drug, some patients do much better with "Perolysen", or with the more recently introduced substance "Ismelin". At the recent Asian-Pacific Congress of Cardiology, a majority of the panel members discussing hypotensive drugs regarded "Perolysen" as the drug of choice.

We find the continued failure to list "Perolysen" disquieting, particularly since one of us wrote to the Department of Health some months ago urging its inclusion in the list.

Yours, etc.,

A. E. DOYLE.
R. FRASER.

Department of Medicine,
University of Melbourne,
Melbourne, Victoria.
November 4, 1960.

SIR: Today I saw a patient with Bell's palsy. I advised a course of cortisone and, having just received my "Notes for Medical Practitioners—Operative from 1st of November, 1960", looked to see whether the list of restricted pharmaceutical benefits would cover his case. It did not, so I tried to explain that cortisone seemed to be restricted mainly to life-saving conditions. With a face that was metaphorically and literally wry, he replied: "The Government—life-saving but not face-saving!"

Yours, etc.,

VOLNEY BULTEAU.

R.P.A.H. Medical Centre,
100 Carillon Avenue,
Newtown, N.S.W.
November 1, 1960.

HYPOGLYCÆMIC EFFECT OF CHLORPROPAMIDE.

SIR: In your issue of October 1, 1960, you presented a case report from Dr. D. S. Pryor, of Newcastle, describing a case of hypoglycæmia resulting from an overdose of chlorpropamide ("Diabinese"). The patient, while under the influence of alcohol, had taken an unspecified number of "Diabinese" tablets and the resultant hyperglycæmia lasted beyond twenty-four hours, responding, however, quite satisfactorily to the administration of glucose.

I venture to suggest that the manner in which this case was reported may give rise to a good deal of quite needless apprehension amongst both doctors and diabetic patients who are currently using or who may in future intend to use chlorpropamide for the control of diabetes. Insulin lowers the elevated blood sugar in the diabetic. If the dose is correct, the blood sugar is reduced to a normal level. If the dose is excessive, the blood sugar is reduced too far and clinical symptoms associated with hypoglycæmia occur. Chlorpropamide in suitable cases lowers the elevated blood sugar in the diabetic. If the dose is correct, the blood sugar is reduced to a normal level. If the dose is excessive, the blood sugar is reduced too far and clinical symptoms associated with hypoglycæmia occur. In other words, both drugs are effective, produce the desired effect if given in correct dosage, and produce disturbance if given in excessive dosage. The difference between chlorpropamide and insulin is that the hypoglycæmia resulting from overuse of chlorpropamide is of slower onset, of milder degree and of longer duration than that following an overdose of insulin.

Nobody feels called upon to issue a public warning against the possibility of insulin causing "hypoglycæmia threatening life". A public warning against chlorpropamide producing a similar effect seems equally unnecessary—more particularly as the effects of overdose of chlorpropamide are slower in onset and much milder than with overdose of insulin. Chlorpropamide in the clinical experience of those who have used it is a notably safe drug—in 150 cases observed in private practice I have yet to experience a moment of anxiety due to the occurrence of troublesome hypoglycæmia. Th manufacturers of the drug make it clear that a dose of 0·5 gramme per day should never be exceeded, and provided that this instruction is carried out, chlorpropamide is perfectly safe.

Doubtless Dr. Pryor felt that by reporting this case he was issuing a timely warning to the profession. I feel however, that the phrasing of his "conclusion' is at least unfortunate and may lead to quite unwarranted prejudice against the use of a drug which in the prescribed dosage is perfectly safe, and which has made much more comfortable and happy the lives of thousands of elderly diabetics, particularly those in whom partial blindness or other physical infirmity makes the injection of insulin a matter of extreme difficulty.

Yours, etc.,

BRUCE HUNT.

37 Ord Street,
West Perth,
Western Australia.
October 31, 1960.

SCHIZOPHRENIA.

SIR: Your annotation on the genetics of schizophrenia struck a respondent chord in both myself and my wife, who is a distinguished P.S.W. Had we not been enjoying an autumn holiday, and on the brink of her confinement, we would have commented upon it in detail. You do not state how much diffusion of population occurred in the two southern Swedish islands; 57,000 is a relatively small sample. If it had remained static for several centuries then its value for such genetic studies would be enhanced. In Monmouthshire the family tie-up in mental diseases is fantastic when dealing with chronic patients. On the other hand, a large mental hospital such as Shenley, serving a London "catchment" area of a million, does not witness brothers, sisters, aunts, cousins in adjacent wards. Metropolitan populations shift and diffuse. The Swedish study seems to be one of these worthwhile pieces of psychiatric research. Unfortunately contemporary psychiatrists are too prone at boarding airliners for foreign parts. They have satchels filled with drool and non-sequiturs, and heads filled with the morose doctrine of our "sick society". Of course the West, under seduction and intimidation, is corrupt up to a point. It needs a bath. But this has nothing to do with endogenously determined mental diseases. Supposing the fantasy of the itinerant psychiatrist is fulfilled by Russian and Chinese paratroops, what then? Dominant genetic factors remain, and the choice then lies between the highest form of humanism or the gas chambers. The "world" psychiatrists are barking up the wrong tree. Means which are inherently evil never produce worthwhile ends.

Yours, etc.,

BARRY MULVANY.

Pen-y-val Hospital
Abergavenny,
Wales.
October 24, 1960.

THE CASE FOR ABANDONING THE TRENDELENBURG POSITION IN PELVIC SURGERY.

SIR: I welcome the criticism and comments of Mr. Gale, and I am gratified to know that he has reached the same conclusion as myself, although by a different method. However, I must still adhere to my original statement, "Packing off the intestines presented no problem, provided the anæsthetist maintained full muscle relaxation during the whole time the abdominal cavity was open", with which Mr. Gale disagrees. I, too, use a Devine retractor, as I am not surrounded by "hordes of clutching hands itching to get a hand inside an abdomen'. It was my experience that when I used the mechanical hand to hold the abdominal packs in position, venous obstruction due to pressure on the iliac veins and inferior vena cava occurred, and I operated in a field which oozed dark blood. Since discarding the hands, I have had no further difficulty with this, but find continued relaxation necessary to retain the packs in position.

I rather gather from Mr. Gale's remarks in regard to post-operative shock that he blames relaxants for it. He may be quite correct, but my observations do not bear out his views. I have not had any cases of shock since aban-

doning the Trendelenburg position, in spite of use of larger doses of relaxants. I have used the same group of anæsthetists both before and after the change of positioning. My operative technique has not altered in any way during the period. The only change has been in the position of the patient, and I have assumed, I think correctly, that this has been the factor in preventing post-operative shock.

Yours, etc.,

231 Macquarie Street, Sydney.
November 7, 1960.

JOHN SWAIN.

CLEFT LIP AND PALATE IN TASMANIA.

SIR: After an excellent statistical survey of genetic factors in "Cleft Lip and Palate in Tasmania", Rank and Thomson conclude that "it would seem unwise that migrant families known to carry this trait should be freely admitted to the community". If this line of argument is pursued to its conclusion (logical or illogical?), it would lead to the exclusion from such countries as Australia (who have been pressed to accept migrants of established lowered medical standards for humanitarian reasons) of those whose blood happens to be Rh-negative, or who happen to have a family history of asthma and hay-fever, or who happen to come from that part of Europe where thalassæmia tends to occur. The dangers are obvious in allowing genetic considerations to influence migration policy to the peril of its more humane ends.

Yours, etc.,

110 Collins Street, Melbourne, C.1, Victoria.
November 5, 1960.

DENIS M. CLARKE.

Obituary.

NEIL ERNEST GOLDSWORTHY.

WE are indebted to PROFESSOR H. K. WARD for the following account of the career of the late Dr. N. E. Goldsworthy.

Dr. N. E. Goldsworthy, Director of the Institute of Dental Research, Sydney, died on September 26, 1960, after a short illness, at the age of 63 years.

Dr. Goldsworthy graduated M.B., Ch.M. at the University of Sydney in 1921. He took the diploma at the London School of Hygiene and Tropical Medicine in 1924. After four years in the Department of Pathology, Cambridge University, under Professor Dean, he was awarded the degree of doctor of philosophy in that university in 1928. On his return to Sydney, he was appointed Senior Lecturer in Bacteriology, a position which he held until he resigned in 1946. During these years he was Bacteriologist at the Royal North Shore Hospital on a part-time basis.

For some years prior to his resignation from the staff of the University of Sydney, he had been working on the problems of dental caries, and when the Institute of Dental Research was formed at the Dental Hospital, Dr. Goldsworthy was appointed as its first director, a position which he held until his death. The new institute was fortunate to obtain the services of such an able, well-informed and interested worker as its director. At first, the Institute was housed in cramped quarters at the Dental Hospital, but when the hospital was rebuilt, spacious and well-equipped accommodation became available. Dr. Goldsworthy leaves behind him a fine Institute of Dental Research with first-rate standards.

Although in his later years Dr. Goldsworthy had turned away from the ordinary paths of medical research, the still unsolved problems of dental caries cannot be divorced from medicine, and this subject was Dr. Goldsworthy's abiding interest. He showed at an orphanage at Bowral that dental caries can be prevented, at the price of a strict dietary discipline. He also worked hard to introduce the fluoridation of water supplies, a procedure which has been shown to cut down the incidence of caries.

A person of wide interests, he was for many years the honorary secretary of the Society of Experimental Biology, and through its lean years he was the head and front of this now flourishing society. His services were recognized by the establishment of the triennial Goldsworthy Lecture, given by distinguished biologists.

Dr. Goldsworthy was the author of numerous scientific papers, which were characterized by their meticulous accuracy and above all by their balance. He was never misled by specious theories unsupported by evidence.

When the Medical Research Advisory Committee of the National Health and Medical Reesarch Council was formed, Dr. Goldsworthy was appointed as the dental representative, and in this position he had the confidence and respect of his colleagues.

Dr. Goldsworthy will be hard to replace, but he bequeaths to his successor a splendid tradition of standards and integrity. He leaves a widow and three sons.

DR. W. W. INGRAM writes: Dr. Neil Goldsworthy was associated with the Institute of Medical Research of the Royal North Shore Hospital, Sydney, practically throughout his whole professional life. He joined the staff in 1930 as part-time "pathologist". In 1931 he succeeded me as Honorary Pathologist when I was appointed Honorary Director. In 1936 he resigned from the honorary staff and was appointed Part-Time Bacteriologist. In 1940 he became Acting Director during my absence on military leave, and was subsequently made also Part-Time Serologist. In 1947 he resigned the positions of Part-Time Pathologist and Serologist when he became Director of the Dental Research Institute. He was then appointed Honorary Consulting Bacteriologist to the Institute.

For many years he was responsible for the immunization of the nursing staff, and he regarded this work as a research project. He devoted much time to the various aspects of disinfection and sterilization, and gave much valuable assistance to the Cross-Infection Committee of the honorary medical staff. A memorandum on skin sterilization prepared by him set the standard of this and other related problems. He was a most helpful Honorary Consultant Bacteriologist, always ready to give advice and practical assistance to the department he had helped to establish. Sir Norman Nock, Chairman of the Board of Directors, has frequently expressed to me his appreciation of Dr. Goldsworthy's splendid reports. When Dr. G. V. Rudd, Research Biochemist, resigned, his place was taken by Dr. M. R. Lemberg. Goldsworthy and Lemberg became great friends and frequently collaborated. It is largely owing to the vital work of Dr. Goldsworthy and Dr. Lemberg that the Institute achieved the prestige it enjoys today.

On the National Health and Medical Research Council and its Medical Research Advisory Committee he represented dental research, and his well-balanced advice will be greatly missed.

Perhaps his greatest service to the scientific life of Sydney was his work for the Pathological Society, which in 1949 became the Society of Experimental Biology; to many it is still known as the "Goldsworthy Society". He was also among those who widened its scope to include the whole field of experimental biology. The society has recognized what he did for it by instituting the "Goldsworthy Lectures", the first of which was given in 1956 by Professor Bonner, the second in 1960 by Professor Dobziausky.

Goldsworthy was a modest and self-effacing man with a loyalty and quiet determination that earned him the respect, admiration and affection of all those with whom he worked. The technical staff of the Institute was devoted to him. There have been few such men as Neil Goldsworthy in the Australian scientific world, and we are grateful that we have had the opportunity of being his associates.

MALCOLM WELD FLETCHER.

WE have received from DR. L. HARDY WILSON the following appreciation of the late Dr. Malcolm Weld Fletcher. This is further to the two previous notices, published in the Journal on September 10 and October 15, 1960.

The obituary of Malcolm Fletcher is not complete without a word of appreciation of his service to his profession as a member of the Branch Council and as President of the Tasmanian Branch of the British Medical Association. Choosing deliberately to serve the Association at a period when his professional life was at its busiest, he spent a happy and successful year as Chairman of the Northern Subdivision. On elevation to the Branch Council, he was soon seasoned to the procedures of that body.

As others have said, his honesty was patent. In debate, although by character conservative, he was ever willing to consider the opposing point of view. Nor were his

personal opinions permitted to restrain his championship of the views of the Subdivision which he represented.

During his term as President, he dealt with the problems of office with characteristic courage, and with a measure of tact which belied his forthright approach and did him great credit. His presidential year was distinguished also by the advent of the Australasian Medical Congress to Hobart. Both he and his wife Janet lent grace and dignity to their positions as leaders of the host State.

He retired from the Branch Council not many months before his death, with the enconiums of his colleagues for six years of valued service. His cheerful presence at Council, and his stimulating companionship during the long drives home, will not be forgotten by his friends in this life.

Public Health.

NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL.

THE following resolutions[1] were adopted at the meeting of the National Health and Medical Research Council held in Canberra in May, 1960.

Medical Research in Australia (1).—That the scope and future policy of medical research in Australia should be examined by an expert committee consisting of Australian representatives nominated by the Medical Research Advisory Committee and that the assistance of one or two overseas experts be enlisted to enable impartial opinion to be put forward during the committee's deliberations. This committee to comprise representation from the Australian National University, Commonwealth Department of Health, Research Institutes, Universities and Clinical Medicine, with power to make other recommendations.

Synthetic Vitamins (2).—That the addition of synthetic vitamins to food be controlled by a general prohibition to which specific exceptions may be made by regulation.

Patent Medicine Advertisements (3).—That section 100 (6) of the *Broadcasting and Television Act* be amended by substituting the following:—(1) A licensee shall not broadcast or televise an advertisement relating to (i) a substance or appliance for which a therapeutic use is claimed, or (ii) a substance, appliance, method or technique for which cosmetic, physiological or anatomical advantages are claimed, unless the text of the proposed advertisement has been approved by the Director-General of Health, or, on appeal to the Minister under this section, by the Minister.

Atmospheric Contaminants (4).—That the schedule of recommended maximum concentrations of atmospheric contaminants for occupational exposures, as recommended by the Industrial Hygiene Committee in March, 1960, should be published as the Australian standards on this subject.

Radio-therapeutic Proposals (5).—That the Australian Atomic Energy Commission be invited to submit to the Chairman of the Council for its evaluation, proposals it has, from time to time, for the production of radio isotopes in the form of grains, wires, rods, discs regular and irregular shapes for radio-therapeutic purposes within Australia.

Medical Statistics (6).—(a) That the certificate which the coroner is required to complete for purposes of registering a death should contain provisions for reporting the cause of death in the form prescribed in the international medical certificate of cause of death. Guidance as to the sequence of causes of death from the medical viewpoint can be obtained from the medical practitioner conducting the post-mortem or, if no post-mortem was required, from the medical practitioner(s) advising the coroner as to the cause of death from the medical viewpoint.

(b) That it would be of considerable assistance, in the interests of accuracy, clarity and uniformity, if a schedule of notes was prepared for the guidance of coroners.

Medical Certificates (7).—So that the essential difference in the information sought of the certifier in the two parts of the medical certificate may be visually accentuated, and in order to avoid the use of Part II (other significant condition contributing to the death, but not related to the disease or condition causing it) as a space to insert spill over information from Part I, it is recommended that: (1) Two lines be provided for the insertion of the cause in *(c)* of Part I. (2) A heavy line be drawn between Parts I and II. (3) The heading—Other significant conditions contributing to the death but not related to the disease or condition causing it—be printed across the certificate, under the heavy line and above the line on which the conditions are entered.

Carcinoma of the Lung (8).—That the Council expresses itself as strongly of the opinion that, cigarette smoking being a contributory cause in the development of lung cancer, Commonwealth and State Departments of Health, local health authorities and educational institutions should devote special attention to a campaign to publicize the risks to health attaching to tobacco smoking. The Council also considers that cigarette and tobacco advertisements on television and radio and in the Press should be subject to strict control to prevent the fostering of smoking by young people.

[1] Reprinted here from the Commonwealth Department of Health's journal, *Health*, September, 1960, by courtesy of that journal.

Medical Matters in Parliament.

HOUSE OF REPRESENTATIVES.

THE following extracts from *Hansard* relate to the proceedings of the House of Representatives.

October 25, 1960.

Canberra: Care of the Aged.

MR. J. R. FRASER: I ask the Minister for Health. Does he recognize that although the present composition of the population of Canberra is what is described as young, the proportion of aged persons in the population is increasing and will increase steeply during the next ten years? Will the Minister inform the House whether any steps are being taken to plan for the establishment either of nursing homes, convalescent homes or geriatric hospitals to cater for the needs of the aging population of this city within the foreseeable future? Will the Minister give what impetus he can to any planning that is taking place?

DR. DONALD CAMERON: I understand that there have been some suggestions for such provisions and some planning is going on. The honourable member can be assured that such proposals will receive from the Department of Health the usual sympathetic consideration.

Telephones for the Blind.

MR. BLAND: Has the Postmaster-General received representations from the Commonwealth Blind Communication Committee regarding concessions to blind persons for the installation and rental of telephones? Is the Minister empowered to grant these concessions by administrative action? If so, will he do what he can to meet the wishes of these grievously afflicted people?

MR. DAVIDSON: Mr. Speaker, over what I confess to be quite a protracted period, I have received representations from a number of bodies and from honourable members regarding the question posed by the honorable member for Warringah. He himself discussed this matter with me previously. I told the House some little time ago that I had had discussions with some of my colleagues who were involved in this matter of the provision of special telephone concessions for the blind, notably the Minister for Social Services and the Minister for Repatriation. It is only within the last week or so that I have been in a position to give a considered reply to the representations made to me. I think the honourable member for Warringah will receive advice of the final result of our discussion quite shortly. That is the position at present. This matter has received very sympathetic consideration, but it is difficult to reach a decision at the present time.

Poliomyelitis.

MR. SWARTZ: I address a question to the Minister for Health. What age groups have been covered in Australia so far in the antipoliomyelitis campaign? Is it intended to extend the campaign to cover the whole of the community as sufficient stocks of Salk vaccine become available? Have experiments been conducted into the breeding of the rhesus monkey in Australia? Is there any further evidence which would indicate the successful use of an oral vaccine for poliomyelitis?

DR. DONALD CAMERON: The age groups so far covered are those up to 44 years. There is now an ample supply of Salk vaccine, and there are no longer any priorities among age

groups. The vaccine is available freely to all the population. So far as I know, there have been no experiments into the breeding of rhesus monkeys in Australia. As to the honourable member's fourth question, it is not considered that there would be any advantage in introducing oral vaccine into Australia. The present injectible vaccine is considered to be highly effective and quite satisfactory.

Notes and News.

Tenth Annual Post-Graduate Course of FOCLA.

The tenth annual post-graduate course of the Federation of Country Local Associations, New South Wales, will be held at Goulburn from March 20 to 24, 1961. The Course Secretary is Dr. B. W. Coombes, McKell Place, Goulburn. Further details will be announced later.

Need for Adult Immunization.

The immediate introduction of a nation-wide campaign to foster adult as well as child immunization against poliomyelitis and tetanus was advocated by the National Health and Medical Research Council at its recent meeting at Canberra. The Council carried a resolution regarding immunization against poliomyelitis which stated that the adult rate of immunization, particularly in N.S.W. and Victoria, was very unsatisfactory. It urged that every means of publicity and education available, at Commonwealth and State levels, be used to bring to the age groups over 20 their responsibility to be immunized. The resolution added: "Because of the present low state of immunity, there is a danger of a further outbreak of poliomyelitis." The Council was informed that arrangements would soon be complete between the Commonwealth and States for the free distribution of Salk vaccine to private doctors. It was hoped that this would greatly encourage adult vaccination.

The Council carried a resolution which stated: "In order to prevent tetanus and to minimize the risks attaching to the use of anti-tetanic serum (after injury) the Council advocates the active extension of tetanus immunization." It was stated that this could be accomplished in the case of adults by a combined tetanus-poliomyelitis vaccine. The Council urged the Commonwealth to take whatever steps might be necessary to ensure that the new quadruple vaccine was available for general distribution by next February. The Council was assured that the Commonwealth Serum Laboratories expected to have the vaccine available in quantity by February 1, 1961.

The Medical Women's Society of New South Wales Annual Prize.

The following are details of the Medical Women's Society of New South Wales Annual Prize.

1. The Medical Women's Society of New South Wales shall award a prize of the value of 25 guineas, open to any medical woman registered in New South Wales.

2. The prize shall be awarded for an original contribution on a subject of medical interest published or ready for publication during that year.

3. In the event of a contribution by two or more medical women in collaboration, the prize shall be divided equally between the contributors. Work done in collaboration with other than medical women may be submitted.

4. The Medical Women's Society of New South Wales shall appoint examiners, and the award will be made on their recommendation.

5. The closing date for entries is February 28, 1961. Entries should be submitted to the Honorary Secretary, The Medical Women's Society of New South Wales, Rachel Forster Hospital for Women and Children, 150 Pitt Street, Redfern, N.S.W.

6. The prize shall not be awarded if either the examiners or the committee of the Society consider that the standard of the work or works is not sufficiently high to justify the award of the prize.

Infected Coconut.

The National Health and Medical Research Council, at its recent meeting in Canberra, recommended that imports of desiccated coconut should be permitted only when there

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED OCTOBER 8, 1960.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	1(1)	1	..	..	..	..	..	2
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	2	..	2
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	1	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	1	..	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	4(3)	10(8)	5(1)	..	..	1(1)	20	1	41
Diphtheria	..	..	..	..	1(1)	..	..	..	1
Dysentery (Bacillary)	..	1(1)	..	..	..	..	1	..	2
Encephalitis	..	2(1)	..	1	..	..	..	1	4
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	139(57)	78(52)	18(5)	15(8)	11(7)	..	1	1	263
Lead Poisoning	..	..	1	..	..	..	..	..	1
Leprosy	..	..	1	..	..	..	3	..	4
Leptospirosis	..	..	1	..	..	..	..	..	1
Malaria	..	..	4(4)	..	1	..	..	..	5
Meningococcal Infection	..	1(1)	..	..	..	..	..	..	1
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	..	..	..	..	6(4)	..	..	7
Puerperal Fever	2	1(1)	1	..	..	..	..	..	4
Rubella	..	17(12)	2(2)	1	3(3)	..	..	..	23
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	4(1)	10(6)	5(4)	4	1	..	..	..	24
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	14(13)	23(18)	10(4)	6(2)	7(5)	2(1)	4	..	66
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

was satisfactory evidence that it had been manufactured under hygienic conditions. The Council was told that in several States great difficulty had been encountered in deciding whether cargoes of coconut were free from harmful organisms. Dysentery infection had been discovered in a number of samples taken, and many consignments had been destroyed, in consequence. However, there could be no certainty that harmful organisms in other consignments had not escaped notice. The Council recommended also that the Commonwealth Department of Health should investigate the practicability of using ethylene oxide gas as an effective means of disinfecting suspect cargoes reaching Australian ports. The meeting was told that fully effective means of manufacturing under hygienic conditions had been developed in New Guinea, with steam sterilization.

New Director of Tuberculosis.

The Minister for Health, Dr. D. A. Cameron, has announced that Dr. Alan King, of Perth, will succeed Dr. Hilary Roche as Commonwealth Director of Tuberculosis.

The Royal Australasian College of Physicians.

EXAMINATIONS FOR MEMBERSHIP.

THE first examination in Australia in 1961 for membership of *The Royal Australasian College of Physicians* will commence with the written examination on Friday, March 10, in capital cities where candidates are offering. Only those candidates whose answers in the written examination have attained a satisfactory standard will be allowed to proceed to the clinical examination. This examination will commence in Sydney on Monday, April 17. If sufficient candidates are offering for examination in Perth, a clinical examination will also be held in Perth on Wednesday, April 26, 1961. Application forms may be obtained from the Honorary Secretary of the College, 145 Macquarie Street, Sydney. Applications should be lodged not later than Friday, February 10, 1961, or in the case of candidates who are domiciled outside Australia or New Zealand, not later than January 9, 1961.

The second examination in Australia in 1961 will commence with the written examination on Friday, August 25. The clinical examination will on this occasion be held in Adelaide, commencing on or about Wednesday, October 4. Detailed information concerning this examination will be published at a later date.

Notice.

ST. VINCENT'S HOSPITAL, SYDNEY: GASTRO-ENTEROLOGY UNIT.

THE next meeting of the Gastro-Enterology Unit of St. Vincent's Hospital, Sydney, will be held on Thursday, November 24, 1960. Dr. S. Goulston will speak on "Gastro-Enterology Units in the U.S.A. and Europe". All medical practitioners are invited to attend.

Nominations and Elections.

THE following has applied for election as a member of the New South Wales Branch of the British Medical Association:

Burke, Kenneth James, M.B., B.S., 1958 (Univ. Sydney), 30 Gipps Road, Gwynneville, Wollongong.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Babajews, Alibaba, M.D., 1937 (Univ. Baku), licensed under Section 21C (4) of the *Medical Practitioners Act*, 1938-1958; Burke, Kenneth James, M.B., B.S., 1958 (Univ. Sydney); Hardacre, Leslie Brian, M.B., B.S., 1956 (Univ. Sydney); Kwok, Frank Yam Wang, M.B., B.S., 1959 (Univ. Sydney); Scotton, Roderick Warren, M.B., B.S., 1958 (Univ. Sydney).

Deaths.

THE following deaths have been announced:

BLOCH.—Michael Bloch, on October 31, 1960, at Melbourne.

DENNIS.—Charles Edgar Dennis, on November 6, 1960, at Melbourne.

Diary for the Month.

NOVEMBER 22.—Tasmanian Branch, B.M.A.: Southern Subdivision.
NOVEMBER 22.—New South Wales Branch, B.M.A.: Hospitals Committee.
NOVEMBER 23.—Victorian Branch, B.M.A.: Branch Council.
NOVEMBER 24.—South Australian Branch, B.M.A.: Scientific Meeting.
NOVEMBER 24.—Tasmanian Branch, B.M.A.: Northern Subdivision.
NOVEMBER 24.—New South Wales Branch, B.M.A.: Branch Meeting.
NOVEMBER 25.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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